MORBID CONDITIONS

OF

THE URINE

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DEPENDANT UPON

DERANGEMENTS OF DIGESTION

BY

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WITH RESPECT AND ESTEEM

PREFACE

In the present work it is intended to confine the attention to those urinary derangements which are the result of chemical changes occurring within the body, as distinct from those morbid conditions of the urine which are directly associated with disease of the renal organs or of the genito-urinary passages, or those which, like diabetes and temporary albuminuria, are the result of disturbance of the circulation in the hepatic and renal vessels.

During the last twenty years physicians have paid but little regard to these derangements, which during the earlier part of the century were the subject of exhaustive research and furnished the materials for keen discussion and controversy. Three causes may be assigned for this neglect. In the first place the attention of pathologists has of late years been almost exclusively directed to histological research. Secondly, owing to the dominant position uric acid has assumed in humoral pathology there has been a tendency to refer these derangements to the same category and to speak of them somewhat indiscriminately as connected with "gouty" proclivities, and thus to overlook some of their distinctive characters. Lastly, there is no department of clinical medicine which is generally so perfunctorily performed as the examination of the urine in disease.

As a rule, we are content with determining the presence or absence of albumen or sugar, the nature of deposited matters, and recording the specific gravity and reaction without, however, reference being made to the conditions as regards time, food, &c., at which the urine was passed. Whilst it seldom happens that any attempt is made to determine the actual acidity or the amount of solid matter passed daily, yet it is almost entirely by this means that we can hope to obtain an insight into the nature of the metabolic changes occurring within the body.

But whilst this branch of urinary pathology has been comparatively neglected of late years, physiological chemistry has made considerable progress, and this is especially the case with reference to the physiology of digestion. Not only have recent discoveries elucidated much that was obscure, but they have also opened up new points of view. It is, therefore, with the aid that physiological chemistry now affords us that it is proposed to pass under review the facts connected with the subject of the morbid conditions of the urine dependant on derangements of digestion. Much of the material of which the present volume is comprised has already appeared in the pages of the 'Lancet' during the last five years. The encouragement the author received during their publication in a separate and detached form leads him to hope that now they are arranged in a more systematic manner, they may prove serviceable towards the elucidation of these still difficult problems in chemical pathology.

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CORRIGENDA

On page 11, and again on p. 16, the formula for Acid Sodium Carbonate and Normal Sodium Carbonate should be NaH_2CO_3 and Na_2HCO_3 respectively, and not $NaHCO_3$ and Na_2CO_3, as given in the text.

MORBID CONDITIONS OF THE URINE

CHAPTER I

ON THE FORMATION AND REMOVAL OF ACID FROM THE BODY

Acid and acid salts are continuously entering the blood. (1) They may be introduced into the body from without in the food. The quantity, however, thus derived under ordinary conditions is comparatively small, since nearly the whole of the saline constituents of the food are alkaline, or become so by conversion in the system. Still, a small quantity of acid sodium phosphate is derived from the juice of flesh, and this passes no doubt unchanged into the blood. (2) Acid, too, is generated in the alimentary canal from fermentative decomposition of the saccharine matters taken with the food, or of the amylaceous principles that have been converted into sugar. In health this fermentative process is most active at the lower part of the small intestines, and in the first portion of the large intestine. (3) Lastly, acid is generated in the tissues of the body. Thus, in a condition of inactivity the lymph fluid of all tissues is alkaline or neutral; on activity being evoked the reaction becomes acid. This is well seen in what

follows the contraction of muscles, in which the contraction wave gives rise to sarcolactic, carbonic, and other volatile fatty acids, and probably glycerin-phosphoric acid. Of these acids the carbonic passes directly into the blood in a free state. With regard to the other acids, their distribution and combination with the inorganic bases, likewise set free by the process of tissue oxidation, is so highly complicated that little is known about them. It is probable, however, that the lactic and other organic acids are converted in carbonates, probably acid (bi-) carbonates, and that some portion of the phosphoric acid enters the blood as acid sodium phosphate; since Maly* has conclusively determined the presence of acid sodium phosphate and acid sodium carbonate (bicarbonate), the latter an acid salt with an alkaline reaction.

In spite, however, of this constant entrance of acid into it, the blood of the living body is always alkaline, no doubt because the chief acid salt (sodium bicarbonate) has an alkaline reaction. What the degree of alkalescence of normal blood is has not been determined, but it is probable that, like the temperature and specific gravity, it has certain definite limits which cannot be passed in either direction without causing disturbance of healthy nutrition. In fact, great difficulty is experienced in reducing the alkaline reaction of the blood.† Hoffmann, who fed pigeons for a considerable time on food yielding only an acid ash (yolk of egg), found that however great the tendency of uric acid and of the acid salts of phosphoric acid to combine with bases, yet these were

* "Untersuchungen über die Mittel zur Saürebildung im Organismus." R. Maly. 'Z. für Phys. Chimie,' 1877.

† "Ueber der Uebergang von freien Saürer durch das alkalische Blut in den Harn." 'Z. für Biologie,' vii.

not withdrawn from the alkaline blood, but were evidently withheld to maintain its alkalinity. Lascar,* by introducing diluted mineral acids into the stomach, succeeded in reducing the alkalescence of the blood but not considerably, and the conclusion he arrived at was that the organism retained free alkali with great energy. In some of his experiments the quantity of acid introduced into the stomach would have made the whole animal acid if it had been absorbed and excreted again. From this Lascar infers that the organism possesses certain "regulative mechanisms" which maintain the equilibrium between the acids and alkaline bases in the system. These experimental facts seem to be borne out by what occurs in scurvy. That disease, as has been well established, is brought about by the prolonged and complete withdrawal of the organic vegetable acids and their salts from the dietary of those affected. These organic salts, as is well known, by oxidation in the blood yield alkaline carbonates. Now, the alkaline carbonates are the salts chiefly concerned in maintaining the alkalescence of the blood, and it appears when these are largely withdrawn, as happens when scurvy is induced, the proper degree of alkalescence of the blood is maintained with difficulty, and in order to secure it some other alkaline salt is retained instead of being excreted. Thus, I found, after the withdrawal of fresh vegetable food for eighteen days, the total quantity of phosphoric acid passed in the twenty-four hours was slightly reduced, whilst the phosphoric acid in combination with the alkaline oxides was reduced nearly one half. Again, in a case of scurvy, it was found that the alkaline phos-

* "Zur alkalescence des Blutes." 'Archiv für Physiologie.' Pflüger, 1874.

phates increased rapidly on the resumption of an antiscorbutic diet, although the amount of phosphoric acid ingested was the same in scorbutic and antiscorbutic rations respectively. These two facts pointing to the conclusion that the alkaline phosphates are retained in the system when the alkaline carbonates are withdrawn, and discharged when these are again supplied.* All experiments made on animals with a view to reduce the alkalinity of the blood or to neutralise it have ended sooner or later in the death of the animal, and if the process has been a slow one, the definite pathological changes will be found to have occurred in the blood and tissues, closely resembling the changes found in the bodies of patients dying from scurvy, viz. dissolution of the blood globules, ecchymosis in the heart, blood stains in the mediastinum, gums, and mucous surfaces; whilst the muscular structure of the heart, and the muscles generally, as well as the secreting cells of the liver and kidneys, become granular and even distinctly fatty. Lastly, Dr Gaskell † has shown, experimentally, that a dilute alkaline solution acts upon the muscular tissue of the heart so as to produce a powerful contraction, whilst dilute acid solutions produce an opposite effect, and that the muscle of the smaller arteries are acted upon in the same way. These facts seem to point to the conclusion that one factor at least upon which the constriction of the muscles both of heart and arteries depend, is the alkalinity of the fluid surrounding them. It is not unreasonable, therefore, to surmise that variations of the degree of alkalinity would not be unlikely to lead to disturbances of circu-

* 'Inquiry into the Pathology of Scurvy,' by the Author. Lewis, 1877.

† 'Journal of Physiology,' vol. iii, No. 1, 1880.

lation and so effect a secondary chemical influence on nutrition, as well as a direct one

Acid is discharged from the blood by four channels. (1) By the lungs, (2) the skin, (3) with the gastric juice, and (4) by the urine. The escape of carbonic acid by the lungs is effected by means partly mechanical and partly chemical, since carbonic acid exists in the blood in two conditions, loose and stable. By loose carbonic acid is meant that carbonic acid which is given off to a vacuum, and is physically absorbed as well as retained in solution by the alkaline carbonates and phosphates; this loose carbonic acid escapes from the lungs into the atmosphere in obedience to the law of pressures. On the other hand, the stable carbonic acid is in combination with some base and can only be separated from the blood by some chemical means. How this decomposition is effected is not yet determined. The amount of carbonic acid exhaled by the lungs of a healthy adult has been shown by Dr Edward Smith* to average about 950 grammes in the twenty-four hours. The rate of excretion, however, is not uniform, being subject to external influences such as the amount of bodily exercise taken, the nature of the food, and the effect of the meal hours. Thus, Dr Smith has shown that the ingestion of food produces a marked increase on the elimination. Thus, in a mean of eight experiments, he found the rate of excretion before breakfast to be 6·8 grains per minute, after breakfast 9 grains; before a midday dinner the excretion was 8·6 grains, and was continued at the same rate per minute afterwards; before tea the rate was 7·9 grains per minute, afterwards it rose to 9·5 grains. Dr Smith considers

* 'Transactions of Royal Society,' 1860. "Experiments in Respiration."

the fact that no increase occurred after the dinner meal in his case was owing to his dining before his usual hour, and that the action upon the respiration of the previous meal had not passed off. In some experiments he made with Dr Murie and Professor Frankland an increase was observed. This increase in the exhalation of carbonic acid, or to express it plainly, the acidity of the breath after food, is interesting when taken in connection with the fact that the opposite effect is noticed with respect to the urinary secretion, the acidity of which is depressed by the ingestion of a meal.

In addition to the carbonic acid passing off by the lungs, about six grammes of this gas are exhaled by the skin during the same period. The sweat or fluid perspiration has also a decided acid reaction, which is due to the presence of formic, acetic, and butyric acids. The quantity of acid, however, discharged by this channel has not been determined, it probably varies greatly even in health, and a very considerable amount is excreted when strong exercise is taken; whilst in certain diseases, as acute rheumatism, the quantity discharged by the skin is often enormous.

The gastric juice is always acid, and its acidity has now been incontestably proved to be due to hydrochloric acid—at least, Richet has shown that in the fresh secretion this is the only mineral acid present. Lactic, acetic, and butyric acids are also met with in gastric juice, the result of fermentative changes occurring in the stomach. In certain morbid conditions, which we shall consider further on, they may be considerably in excess of the hydrochloric acid, indeed, that acid may be very scantily secreted,* and thus by causing delay

* 'Du Suc Gastrique chez l'Homme et les Animaux.' Paris, 1878.

in gastric digestion lead to the formation of these organic acids. In many cases of acid dyspepsia it is a matter of importance to determine whether the acid in the vomited matters contains a due proportion of hydrochloric acid or whether the organic acids are in excess. In the former case the acidity will arise from hypersecretion, in the latter from fermentative changes, or both acids may be in excess. In this case the mischief will probably have arisen in the first place from hypersecretion of hydrochloric acid arresting digestion ;* the formation of lactic, acetic, and butyric acids being a consequence of this arrest. Till recently we had no ready means of determining the nature of the acid present in the vomited matters, and therefore uncertainty frequently existed as to the conditions under which the acids expelled were formed in the stomach. Richet, however, has suggested a method by which the nature of the acid can be accurately determined, and has thus supplied us with an additional means of diagnosis in those cases of stomach disease attended with the vomiting of acid matters. His method is based on the fact that if an aqueous acid solution be shaken with ether the latter removes a constant quantity of the acid. This, in the case of mineral acids, is extremely small, but with organic acids the removal is considerable. The specific ratio which exists, after an aqueous solution of acid has been agitated with ether, between the quantity of acid taken up by a certain volume of ether and that which remains in an equal volume of the solution after it has been treated with ether, is called the "co-efficient of partage," a term originally applied by Berthelot. The co-efficient of partage, in the case of mineral acid, is

* Experiments with artificial gastric juice show that the addition of too much acid arrests the digestive action.

high—above 500—because the quantity of acid yielded to the ether is small; the co-efficient for the organic acids is low for the opposite reason. The following example will render the matter clearer: 100 grammes of water containing 11 grammes of lactic acid, and 100 grammes of ether agitated with this solution removes 1 gramme of acid; so when we determine the acidity of the two fluids we find that of the water to be 10 and that of the ether 1. But supposing the degree of dilution to be ten times greater than in the first case, then 100 grammes of water which contains 1·1 grammes of lactic acid, agitated with an equal weight of ether, will yield to the ether 0·1 gramme, and retain 1 gramme, the co-efficient of lactic acid is therefore said to be 10. The co-efficients of many other organic acids have been determined. Some of the most important as having a bearing on animal chemistry are succinic acid $c'=6$, benzoic acid $c'=1·8$, oxalic acid $c'=9·5$, acetic acid $c'=1·4$. So far as concerns one acid in solution the operation is simple enough, but when we have to deal with a mixture of two or more we must have recourse to a series of agitations with ether so that we may separate the acid which is the most readily soluble in ether from the one that is less so. By such repeated treatment of the original acid solution with ether, and recording the co-efficient of partage after each operation, we are able to obtain the true co-efficient of partage for each acid present.

The acidity of human gastric juice varies considerably according to the statements of different observers. Thus Richet,* from numerous observations on a patient after gastrotomy, gives the average acidity as 1·7 with a maximum of 3·4 and a minimum of 0·5 per thousand.

* Op. cit, p. 68.

Schroeder,* from observations made in a female with gastric fistula, records it as low as 0·2. Schmidt,† from experiments on dogs, gives an average of 2·5 and Szabo ‡ with the same animals 3 per thousand. These variations need not be considered contradictory, the acidity of the gastric juice no doubt depending much on the nature of the physiological stimulus that excites it. This supposition receives support from the observations of Schmidt, who found the juice of herbivorous animals had a lower degree of acidity than that from carnivorous animals. One point, however, is certain that the acid is present in a very dilute state, thus confirming the results obtained by experiments with artificial gastric juice, in which a degree of acidity of 0.2 per cent. is found to be most effective.

With regard to the amount of acid withdrawn from the blood by the gastric secretion during the twenty-four hours it is impossible to speak with any certainty, since the quantity of gastric juice secreted during that period has never been definitely ascertained. Grünewald§ in a case examined by him states it as twenty-three imperial pints, but this was undoubtedly under pathological conditions. Parkes‖ considers if we put it at twelve pints we shall be within the mark. Lehmann, drawing conclusions from experiments on animals, concludes that the secretion of gastric juice in the twenty-four hours amounts to one tenth of the whole weight of their body,

* 'Succi humani gastrici vis digestiva.' Dorpat, 1853.

† Bidder et Schmidt, 'Die Verdauungssaft.' Leipsig, 1852.

‡ "Beiträge zur Kenntniss der freien Säuren des menschl. Magensaftes." 'Zeitschrift f. Physiologie Chimie,' i, 1877.

§ Beale's 'Archives of Medicine,' vol. i, p. 270.

‖ "Gulstonian Lecture on Pyrexia." 'Med. Times and Gazette,' 1855, vol. i, p. 333.

this per man would represent something like 14 lbs. avoirdupois. Unfortunately, as Richet well observes, the data on which these calculations are founded are very uncertain, since it is extremely difficult to determine the relative proportion of the true gastric secretion and the mucus mixed with it, and also to make allowance for what passes off accidentally during the experiment by the pylorus, and what is absorbed by the veins of the stomach. Moreover, even if these obstacles should be overcome, the intermittent nature of the secretion would make it difficult to arrive at very definite conclusions.

We must now proceed to consider the manner in which the hydrochloric acid of the gastric juice is separated in a free state from the alkaline blood. It is only recently that an explanation has been offered to account for this seeming paradox. In 1874,* in order to elucidate this point, I made in the laboratory of the Charing Cross Hospital a series of experiments, in which I found, by introducing an alkaline solution consisting of sodium bicarbonate (5 per cent.) and neutral sodium phosphate (5 per cent.) into a small U-tube, fitted with a diaphragm at the bend, and passed a weak electric current through the solution, that in a short time the fluid in the limb connected with the negative pole increased in alkalinity, whilst the fluid in the limb connected with the positive pole became acid from the formation of acid sodium phosphate. Now, one of the chief salts in the blood is undoubtedly sodium or potassium bicarbonate—an acid salt with an alkaline reaction, and neutral sodium phosphate has also an alkaline reaction. The decomposition which occurs between them may be represented as follows:

* 'Lancet,' p. 29, July 4th, 1874.

Acid Sodium Carbonate. Neutral Sodium Phosphate. Normal Sodium Carbonate. Acid Sodium Phosphate.

$$\overbrace{Na, H, CO_3}^{2} + \overbrace{Na_2, H, PO_4} = \overbrace{Na_2HCO_3} + \overbrace{Na, H_2, PO_4}.$$

The above reaction explains the presence of acid sodium phosphate in urine. To account for the formation of free hydrochloric acid in the gastric juice, sodium chloride is substituted for the neutral sodium phosphate, the decomposition in this case being

Acid Sodium Carbonate. Sodium Chloride. Normal Sodium Carbonate. Hydrochloric Acid.

$$\overbrace{Na, H, CO_3} + \overbrace{Na, Cl} = \overbrace{Na_2, CO_3} + \overbrace{H, Cl.}$$

Maly,* however, who subsequently investigated the subject with great care, has come to the conclusion that the hydrochloric acid is derived from the decomposition of neutral sodium phosphate with calcium chloride, thus

Neutral Sodium Phosphate. Calcium Chloride. Tricalcic Phosphate. Sodium Chloride. Hydrochloric Acid.

$$\overbrace{2\,Na_2, H, PO_4} + \overbrace{3\,Ca, Cl_2} = \overbrace{Ca_3, PO_4} + \overbrace{4\,Na, Cl} + \overbrace{2\,H, Cl.}$$

Practically, it matters little which view we adopt, since all the salts named are present in the blood; the important fact being, that out of the body a weak electrical current will separate the acid from its base. Whether the decomposition occurring in the body is due to the same agency must for the present remain a matter of conjecture. Still, the experiment of Professor Dubois Reymond, made with an extremely sensitive galvanometer, which shows that there are no two parts of the body whose electrical condition is precisely the same, and that the differences between them are greater

* 'Zeitschrift f. Physiolog. Chimie,' p. 174, 1877.

in proportion to the difference in activity of the vital processes which are being carried on in them, makes such an hypothesis plausible,* whilst the interesting discoveries made by Dr Burdon Sanderson, that electrical disturbance takes place during contraction of the leaf of the *Dionæa muscipula*, or Venus's fly trap, points to the same conclusion.

Whatever be the nature of agency that effects the decomposition, it must be a powerful one to effect the separation of hydrochloric acid from bases for which it has such a strong affinity as soda or lime. The decomposition, however, once effected in the blood, there is no difficulty in explaining the presence of free hydrochloric acid in the stomach, since Graham showed many years ago that this acid possesses high diffusive power, and passes from a mixture through a dialyser with great rapidity.

Acid also leaves the body by the urine, since the reaction of healthy human urine collected during a period of twenty-four hours is always acid. This acidity is reckoned as oxalic acid, that is to say, in determining the amount present we use a solution of sodium hydrate standardised so that each cubic centimètre represents ·01 gramme of oxalic acid. The degree of acidity of the twenty-four hours' urine in well-fed adults is generally equivalent to two grammes of oxalic acid.

Now, although the reaction of healthy human urine collected throughout the twenty-four hours is acid, yet if separate samples of the urine passed during this period be taken, considerable variations in the character of the reaction will be observed. The constancy with which these variations occur under different diurnal physio-

* Dr Poore, 'Text-book of Electricity in Medicine and Surgery.' Smith, Elder, and Co., 1876.

logical conditions was first studied by Dr Bence Jones. That physician pointed out that the acid reaction of the urine increases and diminishes inversely with the secretion of the gastric juice. He found, by examining the urine at short intervals during the day, that an increase of acidity was observed in the urines passed before meals, and that a decline in the acidity occurred shortly after food had been taken, and acid was consequently withdrawn from the system; its maximum decline being attained in about three hours, when the acidity begins to rise. In some instances not merely was there depression of the acidity, but the urine became neutral and even alkaline. These observations of Dr Bence Jones have been repeatedly confirmed by subsequent investigators; and the ebb and flow in the intensity of acid reaction of the urine, to which the term *alkaline tide* has been aptly applied, is a recognised physiological fact, though explanations different from that offered by Dr Bence Jones have been advanced to account for the phenomenon. Dr Roberts,* for instance, is disposed to attribute the occurrence of the alkaline tide after meals to a different cause—namely, to the entrance of the newly-digested food into the blood. For if, as he says, the normal alkalescence of the blood is due to the preponderance of alkaline bases in all our ordinary articles of food, a meal is *pro tanto* a dose of alkali, which must, for a time, add to the alkalescence of the system, and consequently of the urine. Dr Bence Jones's view receives considerable support from clinical and physiological experience. Since in those cases attended with frequent vomiting of intensely acid fluid it has often been noticed that the urine passed immediately after the ejection of

* "A Contribution to Urology." 'Memoirs of the Manchester Lit. and Phil. Soc.,' 1859.

the fluid becomes alkaline; the same effect is produced in dogs experimentally when pounded glass or other indigestible substance is introduced into the stomach to provoke the secretion of the gastric juice, which is withdrawn as soon as secreted by washing out the stomach with water by means of a stomach-pump, showing in both instances that the alkalinity of the urine was caused by the withdrawal of acid from the stomach, and not by the addition of alkali to the blood. That the ingestion of food, especially vegetable food, contributes, in a slight degree, in the production of the alkaline tide, is very probable, but that it is mainly concerned in the phenomenon is out of the question, otherwise the alkalinity of the urine would be in direct proportion to the quantity of food ingested, which is certainly not the case. Indeed, the acidity of the urine can be depressed, and even rendered alkaline, otherwise than by the withdrawal of acid from the stomach, or by the ingestion of food. And it is this circumstance, hitherto unexplained, that has rendered many physiologists unwilling to accept Dr Bence Jones's as a complete solution of the phenomenon. Dr Hermann Weber* some years ago observed that whilst breakfast decidedly had an influence in lowering the acidity, yet when he went without that meal the acidity was still lessened, though not to so great a degree. This observation of Dr Weber I have repeatedly been able to confirm, the mere act of rising always producing a decided depression in the acidity of the urine. The use of the cold douche, or sweating in the vapour bath, both have the same effect, quite independently of food or the activity of the stomach.

There is another channel, however, by which acid is

* Professor Parkes, 'On the Composition of the Urine in Health and Disease,' p. 55. Churchill, 1860.

withdrawn from the blood besides the gastric secretion, and that is by the lungs. In the explanations hitherto advanced to account for the phenomenon of the alkaline tide in the urine this fact has not received attention. Dr Edward Smith, in his researches 'On the Elimination of Carbonic Acid,' has, as we have seen (p. 6), showed conclusively that the exhalation of carbonic acid by the lungs is increased by food and diminished by fasting, and that the amount exhaled during sleep is considerably less than is set free in the waking state. It therefore happens that the time when most carbonic acid is being exhaled corresponds with the time when observers have noticed a decided diminution in the acidity of the urine, whilst the circumstances that diminished the exhalation of carbonic acid—namely, sleep and fasting, are attended by a rise in the acidity of the urinary secretion. The following table gives the average result of several observations made by myself to determine the ebb and flow of the tidal variations in the acidity of the urine.

Time.	Total acid as oxalic acid.	Acidity per hour as oxalic acid.
11 p.m. to 8 a.m.* . .	1·14 grm.	0·12 grm.
8 a.m. to 11 p.m. . .	0·21† ,,	0·07 ,,
11 p.m. to 1 p.m. . .	0·40 ,,	0·20 ,,
1 p.m. to 4 p.m. . .	0·11 ,,	0·03 ,,
4 p.m. to 7 p.m.* . .	0·29 ,,	0·09 ,,
7 p.m. to 11 p.m. . .	0·07† ,,	0·02 ,,

The acid reaction of the urine is chiefly, if not altogether due to the presence of acid sodium phosphate.

* Breakfast at 8.30 a.m.; lunch at 1 p.m.; dinner at 7 p.m.

† These samples were sometimes neutral, rarely alkaline.

and occasionally to an excess of acid salts of hippuric and uric acids. I have already (page 10), when speaking of the presence of free hydrochloric acid in the gastric juice, showed how the seeming paradox of the separation of an acid secretion from an alkaline fluid like the blood can be explained. And I pointed out, in the case of urine, that it was the result of the decomposition of a salt with an alkaline reaction but having an acid constitution, like sodium or potassium bicarbonate with another alkaline salt, the neutral sodium phosphate, thus

Acid Carbonate.		Neutral Phosphate.		Normal Carbonate.		Acid Phosphate.
Na, H, CO_3	+	Na_2, H, PO_4	=	Na_2, CO_3	+	Na, H_2, PO_4.

Maly* believes that acid sodium phosphate as well as hippuric and uric acid exists in a free state in the blood, and that the reaction of that fluid remains alkaline on account of the preponderance of alkaline salts. He has shown that if an alkaline mixture containing neutral sodium phosphate and acid sodium phosphate be placed on a dialyser, the acid salt passes into the surrounding distilled water; hence he considers the excretion of acid urine through the renal parenchyma to be simply a process of dialysis.

Maly's explanation has the merit of simplicity, but it does not wholly account for many of the phenomena connected with the variations in the reaction of the urine. If, on the other hand, the view that the acidity of the urine is caused by the reaction between acid sodium carbonate and neutral sodium phosphate be accepted, it will explain another paradox which has

* Op. cit.

been observed by Bence Jones,* Beneke,† Parkes,‡ and myself,§ to occur after the administration of the bicarbonates (acid carbonates) of ammonia, potash, and soda, under certain conditions, viz. causing of an increased acidity of the urine. This point will, however, be more fully referred to when we consider the action of alkaline remedies in the treatment of dyspepsia.

So long as the discharge of acid from the system passes off regularly, and is distributed in normal proportion among the secretions concerned in its removal, its presence on the mucous surfaces with which it comes in contact is unfelt. When, however, the production of acid is excessive, or the distribution of the acid among the various secretions is irregular, so that one becomes more highly charged with acid than the others, then the secondary effects due to "acidity" make themselves manifest. These, when the formation of acid is only slightly in excess, or is only temporarily induced by casual disturbances, may be limited to slight heartburn in the case of the stomach, some itching or nettle-rash of the skin, a little bronchial catarrh, or some degree of irritability of the urinary passages. When, however, the formation of acid is excessive or long continued, the secondary diseases it gives rise to become formidable in their nature. Attacks of acute dyspepsia, accompanied with paroxysms of pain, cramp, vomiting, and diarrhœa, so severe and often so long continued as to reduce the patient to the utmost stage of prostration. Intractable skin diseases, like lepra, psoriasis, and

* 'Philosophical Transactions,' 1850, part 2, p. 673.

† 'Archiv des Wissenschaftlichen Heilkunde,' 1854. "Studien zur Urologie," p. 444.

‡ 'Composition of the Urine in Health and Disease,' p. 297, 1860.

§ 'Lancet,' Nov. 9th, 1878.

eczema, severe asthmatic paroxysms and chronic bronchitis, frequent attacks of gravel and other renal and urinary affections. Excessive formation of acid, determined probably by certain textural and neurotic conditions, is very likely the cause of the severe inflammation of the structures in and around joints, such as we witness in gout and in attacks of acute rheumatism. Indeed, an over-acid state may be considered a predisposing as well as an exciting cause of both these diseases, since the nutrition of the tissues undoubtedly becomes impaired* by the supply of faulty nutritive material, and so the conditions which favour an attack of acute gouty or rheumatic inflammation are developed.

These are the most palpable and direct manifestations of an outburst of an over-acid state, but there are many other ailments, such as palpitations and flutterings of the heart; exaggerated pulsations of large arteries; irregularities and intermissions of the pulse; aching pains in the limbs; burning patches; neuralgia; megrim; vertigo; noises in the ears; depression of spirits, sleeplessness &c.; which many writers describe as arising from irregular manifestations of the gouty state, and which Dr Murchison,† with an equal show of reason, refers to disorder of the liver, but which, without committing ourselves to any definite theory, may be conveniently considered as arising from an accumulation of acid in the system when they occur in persons who have no claim to be considered gouty, nor in whom any

* This is well shown in changes which take place in scurvy, a disease closely allied in many respects to gout and rheumatism, and which develops after the withdrawal for some length of time from the blood of the alkaline salts supplied by vegetable food.

† 'Croonian Lectures.' "On Functional Derangements of the Liver." 1874.

marked disturbance of hepatic function is noticed. One point that should be considered with reference to these affections is their extreme motility—the paroxysmal nature of their onset, the suddenness with which they disappear or transfer themselves from one region or organ to another. These sudden changes afford additional support to the view that these derangements are caused by chemical alterations in the quality of the blood, since we notice similar variations within physiological limits in the secretions of various organs, a certain ebb and flow, as it were, dependent on conditions affecting their functional activity. And when we proceed to reflect on the vastness and complicity of the chemical circulation going on in the body, a circulation the importance of which was little considered till Professor Parkes drew attention to it in the 'Gulstonian Lectures' of 1855,* we can hardly wonder if a pathological check occurring to the elimination of matters ready for their discharge by their natural passage causes an outbreak in another, directed by the same influence that regulates the delicate chemical variations which take place within physiological limits.

* 'Med. Times and Gaz.,' 1855, vol. i, p. 333.

CHAPTER II

DYSPEPSIA USUALLY ASSOCIATED WITH AN ACID CONDITION OF URINE (ACID DYSPEPSIA)

The mucous membrane of the stomach furnishes two secretions: one, which is continuously secreted during fasting, alkaline in reaction, thick and tenacious in consistence; the other, the gastric juice, thin, limpid, and acid, which is only secreted when a stimulus is applied to the walls of the organ. In health the quantity of gastric juice secreted from the walls of the stomach apparently depends more on the general requirements of the system than upon the quantity of the food introduced into the digestive cavity. In disease both the quality and the quantity may be considerably altered. The observations of Dr Beaumont on the stomach of Alexis St Martin showed that in febrile conditions of the system, occasioned by whatever cause, the villous coat becomes red and dry, and the secretions become diminished, and when this condition is considerable no gastric juice will be evoked by the alimentary stimulus. These observations of Dr Beaumont have been confirmed by Blondlot and Cl. Bernard. On the other hand, it has been shown experimentally that under certain nervous influences the secretion is considerably increased. The conditions under which this takes place are not, however, well understood, because the channel by which they are

conveyed has not been definitely determined. Bernard* found that section of the vagi during digestion caused the reddened mucous surface to become pale, whilst irritation of the nerves, or section of the fourth ventricle, above their origin produced dilatation of the gastric vessels, and induced an abundant secretion of gastric juice. Rutherford† also found that the gastric membrane flushed during digestion, became pale when the vagi were cut, and that stimulation of the central end of either nerve caused reddening of the gastric membrane, whilst irritation of the peripheral end produced no constant effect. Lastly, it has been found that when all the nerves that supply the stomach have been divided, gastric juice of normal acidity and digestive power will still be secreted when a stimulus is supplied to the mucous surface of the stomach, alkalies and dilute alcohol being among the most potent, which shows that the nerve centres on which the secretion depends exist in the walls of that organ. From a consideration of the foregoing facts, it is probable, therefore, that when hyper secretion occurs pathologically it is connected with either direct or reflex irritation of these nerve centres. This may be produced either by a morbid condition of the blood, such as may result from an excess of acid developed or retained in the system, in a gouty state, or the taint of malarial poison, or by actual disease of the stomach itself, especially those forms in which the deeper structures are involved, or by disturbance in the other organs conveyed to the nerve centres of the stomach by reflex agency.

Chomel‡ has described an acute affection, which he

* 'Lect. Syst. Nerv.,' vol. ii, pp. 438 and 461.

† Rutherford, 'Phil. Trans. Edin.,' xxvi, 1870.

‡ 'Des Dyspepsies,' p. 144, Paris, 1857.

terms "*la dyspepsie acide grave*," in which it would almost seem as if the whole body turned acid. The disease apparently commences like an ordinary attack of gastric catarrh, but so severe are the symptoms that the patient speedily becomes prostrate and has to keep his bed. There is frequent vomiting of acid matter tinged with yellow-coloured bile, the saliva is acid, and the sourness of the breath so marked that the air of the chamber becomes tainted with it. There is obstinate constipation. After a time the character of the vomit changes from yellow to green bile, which, after persisting a considerable number of days, moderates, the pulse, however, increasing in frequency, with usually a considerable elevation of temperature. At this period certain nervous symptoms develop, headache accompanied by hallucinations, passing gradually into coma, in which in the majority of cases the patient dies. The duration of the disease was from thirty to forty days. Chomel first noticed the affection after the cholera epidemic of 1832, but since then he has repeatedly seen cases. Dr Wilson Fox* also relates that during the cholera outbreak in London in 1866, he was struck with the frequency of subacute inflammatory affections corresponding in their symptoms to those of "*embarras gastrique*," and he also noticed a similar frequency during the autumn of 1871, a year in which cholera was prevalent in Europe but not in England. Last autumn I saw a case which ran a course very similar to those described by Chomel, and, as it presents features of interest, I briefly summarise some of its characteristic details.

A gentleman, about fifty years of age, a *bon vivant*, and of robust habit, and who at the time his illness commenced was in good health, was seized one night (Oct.

* 'Diseases of the Stomach,' p. 100, 3rd edit., 1872.

16th), after dining out, with a feeling of weight and oppression at the chest, which gradually increased till it became unbearable; he then began to vomit, and brought up a large quantity of undigested food and acid fluid. This vomiting was encouraged, and a dose of calomel, followed by some sulphate of magnesia, was ordered. This had no effect, although it was repeated, and other purgatives tried besides, and enemas administered night and morning; it was not till the seventh day that the bowels were opened, and then only to a slight extent. Throughout the illness the bowels remained obstinately constipated, and were only relieved by the action of medicine. The urine was scanty, of a cherry colour, clear, and deposited no urates or uric acid, free from albumen, but highly acid. The vomiting continued almost incessantly for four days, and then gradually ceased, during which time he took only iced Appolinaris water with milk, a tablespoonful at a time. On the fifth day he was able to take a little beef tea, and by the end of the week a little minced chicken. He went on satisfactorily for two or three days after this, when he was seized with a most persistent and troublesome hiccough, which lasted about thirty-six hours, then he began to bring up a small quantity of acid fluid whenever he took nutriment, which consisted of teaspoonful doses of Brand's essence of beef and milk with Appolinaris water. About this time the pulse became very rapid in its action and irregular. The urine still scanty, excessively acid, and highly coloured. Bowels obstinately constipated. Almost every remedy was tried to check the sickness, and some seemed to succeed for a short time and then lost their effect. Equal parts of champagne and Appolinaris water iced stayed with him best. A sixth of a grain of

morphia was given three times a day. He went on in this state for a fortnight or three weeks from the commencement of the illness, during which time he had been quite sensible; on the twenty-first day, however, his nurse reported that he had passed a restless night, and in the morning during her absence he got out of bed and was unable to get back again. On her return she found him talking excitedly and fancying there were people in the room, &c. For some reason or other the usual dose of morphia had been withheld the preceding night. On giving him this he became quieter, and with a second dose he became quite rational. The vomiting, which up to this time had been glairy and colourless, only sometimes tinged with bile, now became darker, and by the twenty-fourth day distinctly contained blood. The abdomen was flat, not tender on moderate pressure, nor was pain at all complained of. The emaciation was considerable; the skin harsh and dry and of a yellow-brownish hue; temperature usually below 98° F., but occasionally towards evening running up to 100° F. or 101° F. The amount of vomit discharged during the twenty-four hours nearly filled a good sized washhand basin. Turpentine was now given, and after a few doses the blood disappeared from the vomit and the sickness gradually diminished, the tongue became cleaner, the urine more plentiful. On Nov. 20th, the thirty-fourth day of the illness, he was able to sit up for a few hours, and had not been sick for five days. He was still kept on milk diet, and the turpentine mixture given once or twice a day. From this he continued to make satisfactory progress, and when seen six months afterwards was in very good health.

In this case it is difficult to determine precisely the condition which led to this prolonged attack of acid

vomiting. During the first week of the illness the patient seemed to be suffering simply from an attack of acute gastric catarrh. After the relapse of the tenth day the character of the vomit was entirely different to what was noticed at first, and there seemed to be more constitutional disturbance. Whilst the case was in progress I thought that possibly the severe attacks of gastric catarrh had evoked some latent organic mischief, and that the irritation of the nerve centres in the walls of the stomach was the cause of the discharge of acid. The complete recovery of the patient negatived this hypothesis. It seems therefore the attack may be referred to a "gouty condition," or an outburst of an over-acid state of the system.

Vomiting of acid fluid sometimes occurs in persons who have been exposed to the influence of malaria, even after other evidences of malarial poisoning have passed away. Dr Fenwick,* who was the first precisely to note this condition, remarks that the vomiting at first only troubles the patient early in the morning, but by degrees it becomes more constant, occurring directly after every meal. In these cases the appetite is always bad, there is loss of flesh, the skin sallow, and the lips bloodless; when the nature of the malady is recognised, it will be found to yield to quinine or arsenic. A case that I saw for the late Dr Murchison, in 1877, may be referred to this cause. An American lady, staying at the Langham Hotel, was seized one morning with a rigor, which was speedily followed by sweating; concurrently with the onset of the sweating she complained of intense pain in the epigastrium and the retching of an extremely acid fluid whenever she

* 'On Atrophy of the Stomach and Nervous Affections of the Digestive Organs,' p. 173. Churchill, 1880.

moved in bed, or attempted to take food or drink. There was no evidence of either biliary or renal colic. As the pain was severe, a sixth of a grain of morphia was injected subcutaneously. This relieved the pain, and in a few hours the vomiting ceased. The next day quinine was prescribed, and there was no recurrence of the pain or vomiting. She informed me she had had similar attacks before, that they were always ushered in by fit of shivering, followed by sweating, and that in the States she had suffered from severe attacks of pronounced intermittent fever.

The vomiting of an acid fluid is usually a distressing accompaniment of cancer and ulceration of the stomach. It is derived apparently from two sources: one from hypersecretion of the gastric juice (hydrochloric acid) from direct irritation of the nerve centres of the stomach, the other from acid derived from fermentative changes occurring in that organ (lactic acid). Both acids are usually present together, but sometimes one preponderates more at one time than another. Thus, Dr Golding Bird* states that in a case of scirrhous pylorus he found at one time a quantity of free hydrochloric acid in one pint of vomit equal to twenty-two grains of the pharmaceutical acid, with an organic acid sufficient in quantity to neutralise seven grains of pure potash. At another time the hydrochloric acid had nearly disappeared, and the quantity of organic acid in each pint required for saturation nearly seventeen grains of the alkali.

Nausea or vomiting generally arises at some period during pregnancy. Most frequently it occurs of a morning, or immediately after taking food, but in some cases, in addition to this disturbance in the morning or

* 'Urinary Deposits,' p. 162. Fifth edition, 1857.

at meal times, there is more or less heartburn and flatulence throughout the day, and in severe cases the vomiting becomes incessant. When the sickness occurs only in the morning, or comes on when an attempt is made to take food, the vomit usually consists of mucus and acid fluid, evidently derived from hypersecretion of the gastric juice. When the vomiting is more frequent, and there is much flatulence, lactic acid derived from fermentative changes will also be present. Similar disturbance of the gastric function, the effect of reflex nervous influence, is met with in organic disease of the uterus and other organs. In phthisis, vomiting of sour fluid, accompanied with more or less pain, not infrequently occurs towards the end of the disease. In these cases the walls of the stomach seem to have undergone atrophic changes, and the vomiting has been attributed to this condition, but, as Dr Budd* pointed out, one circumstance incompatible with the idea that the vomiting is altogether due to these changes, is that the changes of structure found after death do not necessarily correspond in degree with the severity or duration of the gastric symptoms. Many forms of kidney disease, such as chronic interstitial nephritis, tubular nephritis, and suppurative nephritis, are frequently attended with nausea, if not actual vomiting. In these cases, as in phthisis, there are usually changes to be found in the mucous membrane of the stomach, which some authors consider sufficient to account for this symptom. It must be borne in mind, however, that nausea and vomiting when present are often quite early symptoms and disappear for long intervals, perhaps only to be observed again towards the termi-

* 'Organic and Functional Disorders of the Stomach,' p. 187, 1855.

nation of the case. The acid of the vomit thrown up during the sickness caused by the passage of biliary and renal calculi, has been shown by many observers to be hydrochloric acid, the acid of the gastric juice, and my friend Mr M. Beck has informed me that patients suffering from chronic bladder affections are frequently troubled with so-called "bilious attacks." Reflex vomiting of an acid fluid is very common in children in whom irregular secretion of the gastric juice seems very readily excited when teething or suffering from intestinal worms, and Budd* has pointed out that young children with tuberculous disease of the lung, or with inflammation of the brain, suffer from this gastric disorder more frequently than grown-up persons labouring under the same diseases.

Other forms of nervous disturbance have a powerful influence on the secretion of the gastric juice, among which may be mentioned sudden emotions of grief, fear, or anxiety, overwork, intellectual or physical, or the exhaustion consequent on too prolonged fasting, hysterical conditions, &c. In these cases we have often to deal apparently at one time with a condition of increased at another time of diminished secretion. It is perhaps this irregular performance of the gastric function that accounts for the anomalous dyspeptic symptoms these cases so frequently present.

In typical cases, when the symptoms are well defined, there is usually no difficulty in determining whether the "acidity" arises from excessive or irregular secretion of the gastric juice, or from fermentative changes taking place in the alimentary canal. Professor Wilson Fox† has very concisely stated the chief points of dis-

* Op. cit., p. 199.

† 'Diseases of the Stomach,' p. 22. Third edition, 1872.

tinction between them in relation to flatulence, pain, and vomiting. Thus, in hypersecretion little or no flatulence is complained of, whilst in acidity arising from fermentative changes it is a distinctive symptom. Pain, too, is less urgent in the latter condition than it is in the former, when it is often so severe as to give rise to the suspicion of the existence of organic mischief. It differs also in character. In hypersecretion it occurs on an empty stomach, and is generally relieved by taking food; it varies in intensity from a feeling of craving or gnawing to an intense continued burning sensation behind the sternum. In fermentative dyspepsia the discomfort sets in some time after a meal, and is characterised more by a feeling of distension and weight than actual pain; when pain is felt it is generally of a colicky nature, and referred to the intestines rather than the stomach.* Actual vomiting of acid fluid is common in cases of hypersecretion, whilst in acidity arising from fermentation only a slight regurgitation usually occurs. If, however, vomiting does take place, the matters ejected will be found to contain a considerable quantity of organic acid, chiefly lactic acid, and occasionally torulæ and sarcinæ, and it will occur some time after a meal. In hypersecretion, on the other hand, the vomiting often takes place on a completely empty stomach, or is provoked when only a small quantity of food is taken.

* It is probable that the presence for a short time of even a considerable quantity of acid in the stomach does not cause pain. Since, as Dr Bence Jones has shown, when 81 grains or even 162 grains of dry tartaric acid are taken in four or six ounces of water the acid hurts the mouth and upper part of the food tube, and then ceases to be felt for three hours or more, when it gives rise to griping and colicky pain. The pain attendant on hypersecretion seems to originate in the nerve centres themselves and precedes apparently the discharge of acid.

This acid pyrosis must not, however, be confounded with that form of pyrosis or "water-brash," in which the fluid poured out is neutral or alkaline, and which is probably derived from excessive secretion by the salivary glands. Both forms of pyrosis, however, may be present together, the patient complaining of the discharge of watery fluid at one time and of acid at another.

The reaction of the urine, too, exhibits different characters in the two conditions. In acidity arising from fermentative changes the natural reaction of the urine is diminished, or may even become alkaline, with a tendency to deposit oxalates or phosphates. In hypersecretion, however, the general character of the twenty-four hours' urine is to increased acidity and the deposition of uric acid and urates. If, however, individual samples of the urine be examined, it will be found that great variations in the reaction takes place within short periods of time—the urine at one time being intensely acid, and at another neutral or alkaline, the latter condition being frequently accompanied by considerable diuresis. Thus, in a lady who suffers severely from attacks of megrim, accompanied by the vomiting of a glairy acid fluid, I have frequently noticed, after an attack has just passed off, the urine to be alkaline and deposit phosphates, whilst urine secreted before and during the attacks will be highly acid and turbid with urates. Similarly, in a gentleman, who suffers from frequent attacks of paroxysmal sciatica, each attack lasting from two to three hours, a similar variation in the reaction of the urine is frequently noticed. It has already been observed that irregular secretion of the gastric juice is very readily excited in children (p. 28); so we also find the reaction of their urine undergoes frequent changes in the character of its reaction, even

under conditions when the child may be considered healthy. This temporary alkaline condition of the urine in all probability depends on the withdrawal of acid from the secretion during its discharge elsewhere, since in dogs we find that, after powerfully exciting the gastric secretion and making them vomit, the urine becomes decidedly alkaline. In this respect the temporary alkalinity noticed in hypersecretion differs from the diminution of acidity noticed in cases of fermentative dyspepsia, where, as I shall endeavour to show when speaking of that condition, the alkaline tendency is not caused by any withdrawal of acid, but by the entrance of the organic acids the result of fermentative changes passing into the blood, and by oxidation appearing as carbonates of the alkaline oxides in the urine.

Although the secondary and remote effects resulting from hypersecretion are not so marked as is the case in persons suffering from fermentative acidity, where the continued absorption of lactic acid and other vitiated products of digestion gives rise to considerable constitutional disturbance, still this kind of gastric disturbance does occasion derangement of other organs; whilst the so called "*bilious attacks*" seem particularly associated with it. Thus, a person, after complaining for some hours of frontal headache and nausea, begins to suffer from uneasiness and pain at the pit of the stomach, and shortly after vomits, and continues to do so for some hours, bringing up at first a glairy acid fluid, which becomes more and more tinged with bile, till the patient declares he brings up nothing but "pure bile." After a time the irritability of the stomach subsides, the vomiting ceases, and the next day the patient will be found slightly sallow, which usually quickly passes off. If the attacks are frequent, however, the sallowness never quite

disappears, and the patient always looks "*bilious.*" In this form of biliousness the liver is probably not concerned. The copious discharge of bile does not arise from its excessive secretion, but simply from the emptying of the gall bladder induced by frequent vomiting—the sallowness or slight jaundice being the result of duodenal catarrh, excited partly by the acid and partly by the straining in the act of retching.

In forming an opinion as to which form of acidity we have to deal with in a given case we must remember that the one is very likely to produce the other. Thus, if irritation caused by hypersecretion is long continued, conditions arise which, by impeding the digestion of food, favour fermentative changes; indeed the over-acidity of the gastric juice itself is sufficient to arrest the digestion* of albuminous substances, whilst the irritation caused by the frequent pouring out of a highly acid secretion, and the presence of undigested albuminous food, produces at length catarrh of the mucous membrane of stomach—one of the most potent factors in the production of fermentative dyspepsia. On the other hand, if the

* That the presence of too much acid, or neutralisation, arrests the action of the gastric juice can be shown by a very simple experiment. Place some finely minced muscle, or boiled fibrin, about as much as will lie on a threepenny-piece, in three test tubes, *a*, *b*, *c*. Fill each tube two thirds full of artificial gastric juice (0·1 per cent. acidity). Add to *a* a few drops of strong hydrochloric acid. Neutralise *b* with sodium carbonate solution, 1 per cent. Leave *c* unaltered. Place the three tubes in water, both at temp. 40° C; digestion will alone proceed in test tube *c*. (N.B.—If the mixture in test tube *a*, acidified by the addition of hydrochloric acid, be diluted with water, and if the contents of test tube *b* be again rendered of the same acidity they were before neutralisation, digestion will proceed, showing digestion has only been arrested, not destroyed, by the presence of too much acid, or by neutralisation.)

acidity in the first instance is due to fermentative changes brought about by impeded digestion, hypersecretion of gastric juice will at last often be evoked, from the disturbance of the nerve centres of the stomach produced by the irritation of the products of fermentative change. In these mixed cases it is often very difficult to decide which is the originating condition, a point, however, which it is important to determine if we wish to do more than palliate the more urgent symptoms. We should, therefore, in all cases determine the nature of the acid present in the vomit. This can be done either by chemical analysis, a lengthy and tedious process, or by having recourse to Richet's method of separating the acids by ether and determining their coefficient of partage. If this is high we may be sure that hydrochloric acid is predominant, if low that the acidity is due to the presence of organic acids. If the patient does not vomit, or at the most is only troubled with sour risings, the acidity is probably chiefly caused by fermentative changes.

For the relief of the pain and vomiting which result from the acidity of hypersecretion, opium or mophia are the chief remedies. When the disorder seems to arise from direct irritation of the nerve centres of the stomach itself, four or five drops of liquor opii, or an equal quantity of liquor morphiæ administered with bismuth on an empty stomach, generally succeeds in calming and regulating the digestive functions before many doses are taken. When the disturbance is the result of reflex irritation an injection of morphia ($\frac{1}{6}$th grain) is more efficacious than the administration of the drug by the mouth. When the hypersecretion seems to depend upon the accumulation of acid in the system, a gouty state, malaria, &c., morphia or opium should be given

to check the immediate urgency of the symptoms, whilst appropriate steps should be taken to relieve the system of the cause of the disturbance. In the vomiting of pregnancy Ringer* recommends the administration of drop doses of ipecacuanha wine every hour or three times a day. Ipecacuanha, too, he remarks, is sometimes effective in checking the vomiting from cancer of the stomach, and succeeds sometimes after more commonly used remedies have failed. Tincture of belladonna in twenty-drop doses three times a day, has also been found serviceable in the vomiting of pregnancy. Liquor arsenicalis in drop doses on an empty stomach, often proves very serviceable in the late vomiting of phthisis. In a patient of mine in whom it was tried, after other remedies had failed, the relief that speedily followed its administration was very marked. Oxide of zinc, oxalate of cerium, and nitro-glycerine are remedies often used in sympathetic vomiting, their action, however, is uncertain; when administered they may be advantageously combined with belladonna. The application of a mustard plaster over the epigastrium has often a magical effect in stopping the retching and vomiting. When the excessive or irregular secretion of gastric juice seems to depend on minor forms of nervous disturbance, such as the exhaustion dependent on overwork, hysteria, &c., great benefit will often be derived from the use of the douche, especially of sea water, or a course of brine baths at Droitwitch or at Soden. The application of a cold compress at night over the abdomen has also a wonderful effect in regulating and calming functional disturbance both of the stomach and liver. The diet should be nutritious, easy of digestion; an indigestible meal or even a single tough

* 'Handbook of Therapeutics.' Eighth Edition, p. 409, 1880.

morsel often exciting a severe attack of pain and vomiting. The intervals between the meals should not be too prolonged, nor should the stomach be overloaded at any meal. A little food should be taken the last thing at night, and immediately on waking in the morning. Alcohol and coffee as articles of diet are to be avoided, though iced champagne with Apollinaris water or a cup of strong coffee will often "stay the stomach" when the vomiting is severe. Considerable benefit is often obtained by the use of alkaline mineral waters between the attacks by persons who suffer from this form of acidity.

CHAPTER III

DYSPEPSIA USUALLY ASSOCIATED WITH A NEUTRAL OR ALKALINE CONDITION OF URINE (FLATULENT DYSPEPSIA)

As Frerichs* has well observed, though yeast fungi are continually being taken with the food, as in bad beer or bread, and are thus brought in contact with the saccharine and albuminous matters of the food, which are capable of fermenting in the stomach, fermentation does not occur unless another condition is added. The ferment must have time and opportunity for developing itself. Under ordinary circumstances, it is so rapidly removed from the stomach, together with fermentable material, that the process has no time to commence. The conditions, therefore, that favour the development of fermentation are those which retard digestion either by mechanically obstructing the onward passage of the food, or from an abnormal condition of the digestive secretions, or the indigestible nature of the food itself. From experiments, we learn that under normal circumstances the gases found in the stomach consist of oxygen, nitrogen, and carbonic acid, but no hydrogen, which we would expect to find if the gases of the stomach in health were formed by lactic acid fermen-

* "Rep. Clin. Lect.," 'Med. Times and Gazette,' 1861, vol. ii, p. 410.

tation. It is probable, therefore, that of the gases obtained from the stomach under normal conditions, the first two are derived from the air swallowed with the food, whilst the latter is derived by diffusion from the blood. In the small intestine, however, acetic and lactic acid fermentation commences, as is shown by the preponderance of carbonic acid gas, and the presence of hydrogen.* The steps that occur in this process of fermentation are well shown in the following table taken from Professor Ewald's work on 'Digestion :'

$C_6H_{12}O_6$ *Sugar.*

$2(C_2H_6O)$ *Alcohol* $+ 2CO_2$.	$2(C_3H_6O_3)$ *Lactic Acid.*
$C_2H_6O + O = C_2H_4O$ (*Aldehyde*).	$H_2OC_4H_8O_2 + 2CO_2 + H_4$ (*Butyric Acid*).
$C_2H_4O + O = C_2H_4O$ (*Acetic Acid*).	

The occurrence of this lactic and butyric acid fermentation in the small intestines in health, suggests a way in which the carbo-hydrate constituents of the food

* The following table gives the result of Planer's analysis of the gases of stomach and small intestine respectively ('Wiener Sitzgber. Mathem. naturwiss. Classe,' Bd. xlii, 1860).

	Stomach.		Small intestine.	
Gas.	Meat.	Bread.	Meat.	Vegetable diet.
CO_2	25·20	32·91	40·1	47·34
N	68·68	66·30	45·5	3·97
O	6·12	·79	Trace	—
H	Nil	Nil	13·86	48·69

may become converted into fat; for, by this lactic and butyric acid fermentation, the sugar is converted into members of the fatty acid series. The extent, however, to which this fermentation is carried in health is probably small, since if it occurred largely in the intestine we should, as Professor Foster* observes, have a large quantity of free hydrogen excreted by the lungs or bowels, which is not the case. The fermentative changes reach their highest point in the large intestine, so much so as to render its contents acid, in spite of the alkaline character of the secretion from its walls. Here, in addition to hydrogen, we have a considerable quantity of marsh gas (CH_4) developed with sulphuretted hydrogen (H_2S), from the decomposition of the albuminous and other sulphur-yielding elements of the food.

In disease, however, excessive fermentative changes of the food may occur, leading to the production of enormous quantities of gas and the formation of various intermediate products, as we have seen, such as alcohol, aldehyde, and acetic acid on the one hand, and of lactic and butyric acid on the other. Sometimes it is a large quantity of gas that is formed, at another time an excess of acid. Thus, Ewald† speaks of a patient who pithily observed that "there was sometimes a vinegar factory and sometimes a gas works in his inside," in fact, at one time alcoholic fermentation led to the formation of acetic acid, at another, the butyric acid fermentation produced hydrogen and carbonic acid. It is often difficult to distinguish clinically between the different forms of flatulent distension which arise,

* 'Text Book of Physiology,' p. 242. Macmillan & Co.

† 'Lectures on Digestion,' Prof. C. A. Ewald. Translated by Dr. R. Saundby. Williams & Norgate. 1881.

but we receive considerable aid if we are careful to discriminate between those forms where flatulence is the only symptom and those where it is associated with acidity, and also by taking into consideration the period with regard to digestion at which these symptoms develop. Thus, there are some persons, chiefly females, who, immediately on taking food, complain of flatulent distension without acidity, the wind they bring up is inodorous; in these cases the gas does not apparently result from fermentative changes, but is probably derived by diffusion from the blood under nervous influences. When the flatulency is accompanied by a slight degree of acidity, and sets in about an hour after food, and the risings are simply acid, and the eructations comparatively inodorous, acetic and carbonic acid fermentation of the amylaceous and saccharine materials of the food is indicated. When the risings are distinctly rancid, it is evidence that lactic acid fermentation of the nitrogenous principles is progressing. This form of fermentation is usually the most obstinate and severe, since, as Budd* has pointed out, it may continue independently of food by the decomposition of the mucus in the stomach and intestinal canal, so that flatulence may persist even when the stomach is kept empty.

Among the conditions most active in producing fermentative changes in the alimentary canal, that caused by a state of general debility must be accounted as holding the foremost place. In these cases the propulsive action of the muscular walls is feeble, so that the onward passage of the food in different parts of the digestive tract is slow. In addition, the secretion concerned in the solution of the various constituents of the food are generally defective in quality if not in quantity,

* Op. cit., p. 322.

so that food remains undigested for a considerable time. As atonic dyspepsia is the most frequent of all forms of indigestion, so it is the most easily recognised. The broad, flabby tongue, thinly covered with white fur, with its edges indented by the pressure of the teeth; the feeble action of the heart, the loss of appetite, and feeling of weight and distension, hardly ever amounting to actual pain, generally referred to the chest rather than the epigastrium, and experienced shortly after taking food; the sour risings and eructations from the stomach, occurring from two to three hours after a meal, whilst flatulent distension of the bowels is more or less constantly present, giving rise to sensations of weight, tightness, and soreness over the whole abdomen, but more especially distressing in the right and left hypochondriac regions, form a collection of symptoms with which we are only too familiar.

Conditions of the nervous system, as is well known, have a powerful influence on the digestive process. It is, therefore, not surprising to find when innervation is impaired that dyspepsia frequently results. In some instances, nervous disturbance hastens the passage of aliment through the intestines, so that in this form of dyspepsia we have diarrhœa shortly after food instead of acid eructations, flatulence, and vomiting. In the majority of cases, however, the process of digestion is retarded and fermentative changes ensue. As a rule, the flatulent dyspepsia arising from nervous influences is less pronounced and more variable than in atonic dyspepsia, though if the disturbance be long continued, especially if caused by exhaustion from undue mental strain or depressing moral influences, a condition of general debility will in time be induced. A point of interest to be observed in the dyspepsias arising directly

from disturbance of the nervous system is the rapidity with which the tongue often becomes coated with dense fur, and as rapidly cleans on the subsidence of the exciting cause. Flatulent distension of the stomach and intestines often arise in nervous states of the system, apparently quite independently of any fermentative changes occurring in the alimentary canal. Indeed, it is quite impossible to account for the enormous quantity of gas, which consists largely of carbonic acid, often discharged through the mouth on a perfectly empty stomach by hysterical and hypochondriacal patients, except on the supposition that it is diffused from the blood. Certain neuroses of the vaso-motor system leading to sudden increase of the salivary, gastric, and intestinal secretions, which are discharged by vomiting and purging, must not be confounded with acid eructations and yeasty diarrhœa resulting from fermentative changes of the food. Such discharges are observed in the *crises gastriques* which are associated with ataxic phenomena ; and in *pyrosis* or water-brash, in which the fluid, the reaction of which is neutral or alkaline, is poured out by the salivary glands, or from the mucous surface of the stomach, probably both. As a rule, however, dyspepsias arising from disturbances of the nervous system are dependent generally on a condition of hypersecretion, and the fermentative changes arise secondarily out of that condition.

In organic disease of the stomach, acid fermentation is always present in greater or less degree, according to the situation of the lesion. Thus, in disease affecting the body or cardiac end of the organ, the food may be returned so quickly that fermentative changes have not time to take place, whilst in cases where the obstruction exists at the pyloric orifice, the most severe forms of the

affection are met with, and the quantity of acid matters returned from the stomach are often enormous. Thus, Quincke* relates a case of a woman suffering from dilatation of the stomach the result of stricture of the pylorus, in whom the strong acid vomit amounted to 3000 cc. (about 5 pints) in the twenty-four hours. In catarrhal states of the stomach, whilst the process of digestion is impeded by the scanty secretion of the gastric juice, an unhealthy mucus is poured out which rapidly decomposes and itself undergoing fermentative changes, and which is often ejected from the stomach. This, however, must be distinguished from the insipid fluid retched up in the morning in catarrhal conditions resulting from alcohol. This fluid, as Frerichs has shown, is not formed in the stomach, but is due to the increased secretion from the salivary glands, and the saliva swallowed during the night is simply hawked up in the morning, converted, however, into stringy masses by the action of the acetic acid formed by fermentation, on the mucin contained in the saliva. Another cause giving rise to fermentative changes is an anomalous condition of the digestive secretions. Thus in the case of the gastric juice, it has been shown that too much acid though it hinders lactic acid fermentation furthers the development of yeast fungi and alcoholic and acetic acid fermentation. Fermentative changes may also commence in the mouth; this usually depends upon an acid fermentation of the buccal and oral mucus, but in some cases appears to be due to actual acidity of the parotid saliva.† The influence that diminution or increase in the secretion of saliva has on the general health cannot

* 'Correspondenzblatt f. schweiz Aerste,' 1874, Jahrg. 4, No. 1.

† Astuschawsky, "Reaction des Parotis Speichel bei gesamden Menschen." 'Centralblatt f. d. Med. Wiss.,' 1878, 257.

be stated with certainty, but if, as it has been stated, the alkaline saliva is a powerful stimuli for the secretion of the gastric juice, then a deficiency in its quantity, or perversion in its quality and its reaction, are probably not without influence on the secretion of the latter fluid; whilst such alterations must result in imperfect conversion of the amylaceous principles into sugar, and thus lead to acidity and flatulence. Bile exercises an undoubted anti-fermentative action, whilst also it induces increased peristalsis of the intestinal walls. Diminution of the secretion would therefore allow fermentative changes to take place more readily than would be otherwise the case. Dogs in whom biliary fistulæ have been established, pass much offensive flatus. The effect that disease of the pancreas or derangement of its secretion has in the production of disorders connected with digestion has yet to be studied; there can be no doubt, however, that any disturbance of secretion of an organ which has such a powerful action on starch, fats, and albumins, must make itself felt. There is one point, however, concerning the pancreatic juice we must notice, and that is, its prolonged action on albuminous matters leads to the formation of putrefactive products. Thus, "trypsin," by its action on albuminous matters, converts them into two forms of peptone—anti-peptone and hemi-peptone.* The former undergoes no further change, but the other, after a longer or shorter time, breaks up into other bodies, such as leucin and tyrosin, &c., and by prolonged action in neutral or feebly alkaline solutions, into ammonia, sulphuretted hydrogen, hydrogen, and carbonic acid. So that if the peptones are retained for too long a time unabsorbed in the

* Kühne und Lea, "Ueber die Absonderung des Pancreas." 'Heidelb. Natural Medic. Verhandlungen,' i, Hft. 5.

upper part of the small intestines, flatulence may be caused by the continued action of the pancreatic juice.

Among the causes leading to fermentative changes must be mentioned the diet of the individual. In many cases food is taken in such excess that it is not absorbed, and it then undergoes putrefactive changes in the alimentary canal. As much as thirty pounds of a half putrid mass has been got rid of by purgatives. Parkes instances a case of this kind as occurring among some convicts in Australia, who received from seven and a quarter to seven and a half pounds of food daily; dyspepsia, obstinate constipation, diarrhœa, skin diseases, and ophthalmia were the result. That a too free consumption of saccharine and amylaceous articles of diet will induce this form of dyspepsia there can be no doubt, since simple abstinence from such articles of diet is often sufficient to remove the disorder. Milk, containing as it does the very element for lactic acid fermentation is a frequent cause of this form of dyspepsia. Inordinate tea drinkers also suffer greatly from flatulent dyspepsia; this is caused partly by its influence through the nervous system on digestion, partly by the dilution of the digestive secretions by an ingestion of an over-abundance of fluid, by the action of its tannin on the albuminous principles, and, lastly, though not least, by its being a vehicle for a considerable quantity of milk and sugar. Alcohol, likewise, by inducing gastric catarrh, is one of the most active factors in the production of this form of dyspepsia. Food of a bad quality, itself undergoing fermentative changes at the time of ingestion, such as bad bread, bad beer, and the like, introduced into the stomach, is a cause not to be overlooked. Whilst, in relation to food,

we must insist upon its sufficient mastication and upon regular and well-arranged meal times. A sufficient time being allowed between each meal for its proper digestion, but not so far prolonged as to induce exhaustion. Lastly, climate is an important consideration in these cases, patients suffering from flatulent dyspepsia being greatly benefited by residence on dry soil and in sheltered situations. Thus Prout has observed that certain seasons and certain malarious districts more than others aggravate the tendency towards saccharine mal-assimilation, probably by the induction of a catarrhal state of the digestive organs. Some of the most severe and obstinate forms of this disorder I have met with have been in patients who have resided in malarious districts, and at some time or other have suffered from its influence.

Since fermentative changes give rise to the development of flatus and acid, the disturbances we meet with in this form of dyspepsia are caused by the presence of these abnormal products of digestion and the efforts made to expel them. In the majority of instances almost immediately on taking food a sense of weight and fulness is experienced. Then the feeling of weight is exchanged for tearing, twisting sensations, and cramp-like colicky pains. Severe pain, however, and tenderness on pressure, are not complained of, unless there is also organic disease of the stomach. The heartburn is accompanied by eructations of gas and risings of sour acid fluid, and undigested portions of food; actual vomiting is rare, except in cases of pyloric obstruction. So great occasionally is the acidity of these regurgitated matters, that they set the teeth on edge like the sharpest lemon juice, and as Trousseau observes will often cover copper vessels into which they are placed with

a coating of lactate or acetate of copper. In ordinary cases of flatulent dyspepsia the gas is usually carbonic acid, and the sour risings will be found to contain both lactic and acetic acid, one or other predominating according to the nature of the case. In severe cases of catarrh, especially when much unwholesome mucus is secreted by the walls of the stomach, the lactic acid fermentation is carried on to the production of butyric acid, which being volatile, imparts its peculiar rancid odour to the breath; this is particularly noticeable in the catarrhal condition induced by alcoholism. Intermediate products of acetic acid fermentation are also frequently found in the ejected matters, such as alcohol, aldehyde, and acetone. In the cases in which these products are observed, an algoid growth known by the name of *sarcina*, is generally met with. This growth, however, has no effect in producing those abnormal decompositions of the contents of the stomach, and its presence merely indicates that conditions favorable for its development exists in the stomach.

The disturbances caused by fermentative changes in the stomach are not limited to that organ. The acid products formed in it, together with the undigested residue of the food, pass on into the intestines and excites more or less pain and diarrhœa. Again, fermentative changes may occur chiefly in the intestines and only a slight degree in the stomach. In this case, which is associated with a greater or less degree of chronic intestinal catarrh, a constipated condition of the bowels generally exists: for though there may be frequent loose, slimy, and offensive discharges from the bowels, yet a purge never fails to bring away accumulated masses of fæcal matter. The whole of the intestinal tract may be affected, or only part of it. Some

writers have asserted that the evil effects of fermentative changes are more felt in the small intestines than in the large, and that catarrh of the small intestines is generally associated with oxaluria. The flatulence may distend the whole intestinal tract, but one part of it is generally distended more than another; and circumscribed swellings occur, chiefly in the right and left hypochondriac regions, causing pain over the region of the liver and stomach, spleen, or kidneys, and leading the patient to suspect disease of these organs. But the mischief resulting from excessive formation of acid in the stomach and bowels is not limited to mere disturbance of digestion, injurious effects making themselves manifest on the system and on the general nutrition of the body when the morbid condition has been present for some time. These evils, as Dr Wilson Fox has pointed out, are more marked in cases of acidity arising from fermentative change than from the acidity of hypersecretion. The highly acid fluid containing the imperfectly digested products of gastric digestion passing into the duodenum excites more or less catarrh of that portion of the intestine, and the discharge of bile is interfered with, hence persons suffering with flatulent dyspepsia have usually sallow complexions, complain of pain in the hepatic region, and suffer frequently from so-called "bilious attacks." The absorption of the vitiated products of digestion, together with some of the free acid, produce many general and remote disorders of nutrition, so that a condition of debility and exhaustion is speedily induced.

The urine in cases of flatulent dyspepsia has its natural acidity, as a rule, considerably decreased, that is, it becomes neutral or even alkaline; and in severe cases

* Op. cit.

a persistent deposit of oxalates, associated with peculiar train of nervous symptoms, is generally met with (see Chapter V). This condition of diminished acidity of the urine cannot, I think, be accounted for by Dr Bence Jones's* hypothesis that when the contents of the stomach are most acid the reaction of the urine is least acid, because in these cases the acid is not withdrawn from the system but is formed in the stomach itself. Nor can I accept Dr Roberts's view, endorsed by Dr Wilson Fox, that the alkalinity is due to the addition to the blood of the alkaline bases of the food, since in these cases there is no evidence that more food containing alkaline bases is either ingested or absorbed than in a healthy condition. Indeed, so far from there being any evidence that more solid matters are passing into the system, the opposite is generally observed. One point that I have noticed with regard to these urines is, that they effervesce strongly on addition of acetic or nitric acid, denoting the presence of carbonates. These carbonates are those of the fixed alkalies, potash and soda, since the blue reaction given to red litmus paper is persistent and not evanescent, as would be the case if alkalescence was caused by ammonium carbonate. The alkaline condition, therefore, of the urine in cases of flatulent dyspepsia I believe to be due entirely to the excessive elimination of the carbonates of soda and potash, and this excessive elimination is brought about by three conditions—(*a*) general debility and the feebleness with which the respiratory act is performed, leading to the accumulation of carbonic acid in the system. With regard to this point, it is interesting to note that urine alkaline from the presence of carbonates

* "On the Alkalescence of Urine from Fixed Alkali in some cases of Diseased Stomach." 'Med.-Chir. Trans.,' vol. xxxv, p. 41.

of the fixed alkalies is frequently met with in patients convalescing from acute diseases. (*b.*) Diminished secretion of bile, which is the frequent result of the duodenal catarrh produced by the irritation of the acid contents of the stomach being poured into the intestines, gives rise to an accumulation of alkaline carbonates in the blood, the bile being the chief secretion by which alkaline salts are removed from the body; for though a portion of them are undoubtedly reabsorbed into the blood from the intestines, a considerable proportion of them are discharged with the fæces. Obstruction, therefore, to the discharge of bile leads to their retention in the blood, and consequently being eliminated in greater quantity by the kidney. (*c.*) The acids formed by fermentative changes being of the fatty acid series; these on entering the system are oxidised into carbonic acid, and this uniting with the bases of the alkaline oxides form carbonates of these bodies, and by increasing the alkalescence of the blood will diminish the natural acidity of the urine and even render it alkaline.

The irridescent film, consisting of crystals of ammonium magnesium phosphate, often found on the surface of urine of persons suffering from flatulent dyspepsia, is due apparently to the passage of urine alkaline from fixed alkali into a dirty chamber-pot, and has no special clinical significance. For if we take a sample of normal urine of acid reaction and divide it into two portions and place them both in beakers, each of which contains a drop of stale urine, and then render the portion in one of the beakers alkaline with liquor potassæ, ureal decomposition will set in very much earlier in the beaker containing the alkalised urine than in the one permitted to retain its normal acid reaction, and crystals of triple phosphate speedily form.

Cases of flatulent dyspepsia associated with alkaline condition of urine.

Case 1.—A gentleman, aged 60, consulted me during Dr Murchison's absence from town (August, 1874). He stated that during the past four months he had lost flesh and had suffered considerably from muscular pains, especially in the thighs, with a sense of indescribable weariness. General appearance worn; complexion sallow; conjunctivæ slightly yellow. Complains of palpitation of the heart and shortness of breath. Bowels constipated; much flatulent distension; troubled with frequent micturition, and is frequently awoke early in the morning for this purpose. Physical examination elicited that there was no disease of the heart and lungs. The liver was of normal dimension, and there was no pain in the epigastric or right hypochondriac region. The urine was clear, slightly acid when passed, but became alkaline on boiling, and threw down a filmy cloud of phosphates, which redissolved with considerable effervescence on the addition of *dilute* acetic acid. The specific gravity was normal, 1020, no albumen, no sugar, and there was no excess of either alkaline or earthy phosphates, nor any trace of ammonia. The alkalescence was thus solely due to the presence of carbonates of potash and soda. He was ordered two-drachm doses of Carlsbad salts twice a week, and to take a mixture containing ten drops each of dilute hydrochloric acid and tincture of nux vomica. On August 23rd he called, and said that shortly after commencing the treatment he began to feel better. He has lost the worn expression of countenance, and his complexion is clearer. The sense of weariness, backache, and muscular pain have disappeared, and he has regained

some of his lost weight. His urine is normal in all respects, and the tendency to frequent micturition has quite subsided. He considers himself quite well. Advised him to continue the use of the Carlsbad salts for some time longer, but to leave off the acid mixture. Saw him four years afterwards; he had been free from the symptoms ever since.

Case 2.—A lady, aged thirty-six, the wife of a schoolmaster. Has lately been very anxious about her husband's health and that of her only child. Has lost flesh considerably of late, Suffers much from muscular pain, and especially in the legs; much backache. Bowels constipated; suffers much from flatulence. Worn, anxious appearance; complexion sallow, but conjunctivæ clear. No enlargement or tenderness in the epigastric or right hypochondriac region. Heart and lungs healthy. Urine neutral in reaction; the quantity passed in twenty-four hours amounts to 800 centimètres; specific gravity 1020. The phosphoric acid about normal in quantity, being 2·2 grammes; uric acid 0·32 gramme. No ammonia present. There was no sugar; no albumen. Phosphates were thrown down on boiling, but were redissolved with violent effervescence by the addition of dilute acetic acid. The patient was ordered two-drachm doses twice a week of Carlsbad salts and a mixture containing ten-minim doses of dilute hydrochloric acid and tincture of nux vomica. The patient improved materially under this treatment, but not so rapidly as did Case 1. It was not till she was able to leave home with its cares and anxieties for a while that the improvement in her condition became permanent.

Case 3.—A Cambridge graduate, aged thirty-five,

fellow of his college, who for some months previously had been engaged in arduous mathematical studies. Had suffered for six weeks from despondency, and a sense of indescribable weariness, backache, and muscular pains, chiefly in the legs. Has lost flesh. Bowels constipated; suffers much from flatulence. Micturition frequent; is roused often in the night time to pass water. Fears that he is suffering from diabetes. On physical examination his organs were found healthy. Urine normal in appearance, slightly alkaline in reaction, throwing down on boiling a cloud of phosphates, which cleared up with considerable effervescence on the addition of dilute acid. Phosphoric acid normal in quantity. No albumen, no sugar. No carbonate of ammonia. Ordered two drachms of Carlsbad salts two mornings in the week and a mixture with ten-minim doses of dilute hydrochloric acid and nux vomica. In three weeks' time he reported himself quite well.

Case 4.—A gentleman, aged sixty, whom I saw during Dr Murchison's absence from town. Had spent many years of his life in India, in a Civil Service appointment. Has lately been losing flesh, and suffering much from weariness, with muscular pains in limbs. Bowels constipated, with considerable flatulence. Sallow complexion, micturition frequent. Urine alkaline; phosphates normal, no sugar, no albumen, no carbonate of ammonia. On boiling, the urine deposited phosphates, which cleared up with effervescence on the addition of dilute hydrochloric acid. Ordered Carlsbad salts and a mixture with dilute hydrochloric acid and nux vomica. A fortnight afterwards he reported himself as much better, and in a month he wrote to say he was quite well.

I have also noticed similar conditions in six other cases, but as they all present the same features it is unnecessary to quote them in detail. There was loss of weight, weariness, constipation, flatulence, frequent micturition, more or less sallowness of complexion. Urine alkaline, neutral or faintly acid, effervescing on the addition of dilute acid, with no increased elimination of phosphates nor any trace of ammonia or ammonium carbonate. They all rapidly improved under the same treatment.

In the ten cases under my observation the alkalescence of the urine was clearly due to the presence in excess of the carbonates of soda and potash, and to no other cause, since the blue colour on the litmus paper remained permanent and there was no ammoniacal odour; and the inference may fairly be drawn that the dyspeptic symptoms, in the absence of any other determinable condition, were connected with the presence of these salts in abnormal quantities in the blood.

With regard to treatment, the chief object is to prevent the decomposition of the organic matters of the food in the alimentary canal. Thus, when the disorder occurs in delicate people with feeble digestions, we endeavour, by stimulating the gastric secretion and by giving tone to the muscular walls of the digestive tract, to ensure the solution of the albuminous constituents and the onward propulsion of the food generally before fermentative changes can occur. The former indication is probably best effected in the majority of cases by the administration of an alkali before meals, since Claude Bernard has shown that small amounts of diluted alkali introduced into the empty stomach will provoke a discharge of gastric juice more than sufficient to neutralise it. In the case of liquor potassæ, it is

probable the alkali acts simply as a direct stimulus to the mucous membrane, but when the alkaline bicarbonates are taken, in addition to this action it is probable they add to the acidity of the system, being themselves acid salts, and so improve the quality of the gastric secretion. This action of the alkaline bicarbonates is not, however, based solely upon a consideration of their chemical constitution, but from the effect their administration has on the reaction of the urine. Thus, Dr Bence Jones, in a paper read before the Royal Society, 1850, showed conclusively, from a series of observations, that large doses of sesquicarbonate of ammonia not only did not diminish the acidity of the urine, but actually increased it, as he found that the day when most sesquicarbonate of ammonia* was taken the acidity was higher than it had been any previous day, and that the acidity was still very high on the day following its discontinuance. Four years later a similar observation was made by Dr. W. F. Beneke† with regard to the effect of bicarbonate of soda. And, lastly, Professor Parkes‡ instances a case of rheumatic fever in which the acidity of the urine on the day following the administration of bicarbonate of potash was considerably higher than on the day before it was taken. As the question is of considerable importance with regard to treatment, especially of those affections which are under our consideration, I will briefly give the

* Sesquicarbonate of ammonia is half acid carbonate. It contains the elements of one molecule of normal carbonate and two molecules of acid carbonate. By exposure to air it decomposes and is converted wholly into acid carbonate.

† 'Archiv des Wissenschaftlichen Heilkunde,' 1854; 'Studien zur Urologie,' p. 444.

‡ 'Composition of the Urine in Health and Disease,' p. 297, 1860.

results of some observations* made by myself on the subject (the details of the experiments are appended at the end of the volume), which show that the effect of bicarbonate of potash, taken after food, on the acidity of the urine is different from that when it is administered on an empty stomach. For when taken before meals the acidity of the urine on the day of administration was found only slightly depressed, whilst on the day following the acidity was considerably higher than it was the day the salt was taken. But when administered during the process of digestion the acidity of the urine entirely disappeared, being on two occasions neutral and on one alkaline, whilst on succeeding days there was no marked increase in the acidity of the urine as compared with that of the days preceding the experiment. And the same difference was observable in the hourly variations of the urine, for when the bicarbonate was taken before meals the effect of the alkali passed of at the end of two hours, and the amount of acid passed in the succeeding three hours was nearly equal to what was passed on the day no medicine was taken; whilst when the salt was taken after meals the urine remained alkaline up to the end of four hours after the dose was taken, and no recovery of acidity was noticeable. The result of these observations tends, therefore, to establish the fact that the administration of an alkaline bicarbonate on an empty stomach increases the acidity of the system, whilst its administration after a meal diminishes it. But how is it that these alkaline bicarbonates have such opposite effects? The explanation that has occurred to me as the most probable, and by which the variable effect of these salts on the acidity

* "Effect of Bicarbonate of Potash on the Acidity of Urine," 'Lancet,' Nov. 9, 1878.

of the urine can be best accounted for, lies, as I have already stated, in their chemical constitution, the alkaline bicarbonates being acid salts. Now, the acid reaction of the urine is generally considered due to the decomposition that occurs between an acid or an acid salt and the neutral phosphate of sodium in the blood, acid sodium phosphate being formed, which passes out with the urine.

Now, one of the chief acid salts of the blood is undoubtedly bicarbonate of potash or soda an acid salt with an alkaline reaction. The decomposition which results between these two salts may be represented as follows:

Acid Carbonate.		Neutral Phosphate.		Normal Carbonate.		Acid Phosphate.
NaH_2CO_3	+	Na_2HPO_4	=	Na_2HCO_3	+	NaH_2PO_4.

We therefore need not be surprised to find the administration of an acid salt, if it passes unaltered from the stomach into the blood, causing an increase in the acidity of the urine. And this is, indeed, what happens when a dose of bicarbonate of potash and soda is taken into the stomach before meals, for then, the mucous membrane under normal conditions being either neutral or alkaline, the bicarbonate is absorbed undecomposed into the blood, and causes that increase in the acidity of the urine which has been noted. On the other hand, when the salt is taken during digestion, the acid contents of the stomach decompose it, carbonic acid is liberated, which escapes by the mouth, whilst the alkaline bases pass into the system and render it, and consequently the urine, more alkaline.

With the alkali is generally associated some vegetable bitter. Nux vomica or its alkaloid strychnia is the one

usually selected; serviceable in almost every form of indigestion, it is particularly valuable in the flatulent dyspepsia arising from a state of general weakness and debility. Its extremely bitter taste excites the excretion of saliva, and thus aids in the conversion of the starchy matter of the food. It also possesses antiseptic properties. By its action through the nervous system it gives tone to the muscular walls of the digestive tract, and thus ensures the onward propulsion of the food before fermentative changes occur. The increased muscular contractility it imparts aids in overcoming the attendant constipation and in expelling flatus. Nux vomica is usually well borne, but it sometimes causes headache and a feeling of fulness and irritation in the stomach. In this case calumba may be advantageously substituted. Should there be much anæmia, iron must be given, though it is generally tolerated with difficulty; the best way to administer it, so as to cause the least disturbance, is in the form of steel wine diluted with water, taken once a day at dinner time. If the administration of the alkali before meals does not excite a sufficiency of gastric juice, pepsin and hydrochloric acid should be administered during meals. The hydrochloric acid should not, however, be given in too concentrated a form. The strength of the acid solution which in artificial gastric digestion is found to be most active contains 0·2 per cent. of real hydrochloric acid. This degree of dilution can be obtained by prescribing ten drops of the dilute acid of the Pharmacopœia to be taken in two and a half ounces of water (an ordinary wine-glass).

When the dyspepsia arises from nervous disturbance, and there is little or no debility, and we have no reason to suspect deficiency of the gastric secretion, acids taken

some little time before meals are indicated. Combined with nux vomica they are particularly valuable in those cases when the patient has been long in a depressed state, has suffered much from care and anxiety, or has been over-worked. Either hydrochloric, phosphoric, and nitric acids are usually administered, some cases seeming to be more benefited by one acid than by another. Although our physiological and chemical knowledge respecting the action of acids within the body does not enable us as yet to indicate with precision the cases which will receive the most benefit from the administration of any special acid, or give a reason for its employment, still, speaking broadly, we may say hydrochloric acid seems best suited to that class of cases in which the dyspepsia is associated with an alkaline or feebly acid state of the urine unattended with excessive deposition of phosphates, whilst phosphoric acid should be prescribed in those cases where with alkaline urine there is a tolerably constant deposit of phosphate of lime or triple phosphate.* Nitric or nitro-muriatic acid, on the other hand, seems most beneficial in those cases in which the urine is acid and has a tendency to deposit oxalates and urates, or in which sudden and frequent changes in its reaction occur, especially if these deposits or changes are apparently associated with any disturbance of the hepatic function.

Catarrh of the stomach and intestines may be either

* The value of phosphoric acid in these cases seems to depend on the fact that equal quantities of phosphoric acid have a greater effect in rendering the urine acid than either hydrochloric or nitric, probably because the two latter combine with bases to form neutral salts, whilst the former appears in the urine as an acid salt, the restoration of the normal reaction of the urine in this case preventing the deposition of phosphates.

a cause or consequence of fermentative dyspepsia. For the treatment of this condition nitrate of bismuth is the most efficacious drug we possess. It should be given in large doses (twenty to thirty grains) on an empty stomach. The powder is more efficacious than the liquid preparations. It is well, especially if constipation exists, to give with it small doses of some aperient salt, such as sulphate of magnesia or sulphate of soda. Nitrate of potash, in five-grain doses, may also advantageously be added to the bismuth mixture if the gastritis be of a subacute type. Nux vomica is also very serviceable in chronic gastric catarrh, especially, as Dr Ringer has pointed out, when this condition arises from mechanical obstruction to the circulation, such as occurs in chronic bronchitis, dilated heart, or cirrhosis of the liver. In these cases, as well as in chronic alcoholic catarrh, there is generally associated an abundant flux of gastric or intestinal mucus, which unless removed adds to the existing trouble by itself undergoing fermentative changes. For this purpose the systematic employment of small doses of Carlsbad salts will be found of the greatest benefit. A teaspoonful o the salt dissolved in from ten to fifteen ounces of hot water, as hot as the patient can bear it, should be taken every other morning, an hour before breakfast. This dilute warm saline solution seems to have the power of dissolving and removing a considerable quantity of this abnormal mucus, and carrying it off by the bowels, the motions containing not only fæcal matter, but an offensive and glutinous-looking slime, which often adheres most tenaciously to the sides of the chamber vessel. The cold wet compress is also a powerful agent in the treatment of subacute and chronic gastric catarrh, indeed its employment is advantageous in flatulent

dyspepsia from whatever cause it arises. It should not be applied during full digestion, but towards the end of the process, about three hours after a meal. Thus, if the principal meal of the day be taken at seven in the evening, it may be applied at half past ten or eleven o'clock, before the patient retires to rest. In the majority of cases it can be borne the whole night, patients under its influence enjoying sound repose whose rest had previously been disturbed by bad dreams or distressing restlessness. With delicate and feeble persons it is as well at first to limit the period of application to three hours. This can be done if the compress be applied the first thing in the morning, the patient's stomach being stayed with a small cup of tea and a piece of toast to prevent exhaustion. When the compress is removed the skin should be gently rubbed with a bathing glove or a soft Turkish towel. In addition to relieving abdominal plethora it increases the peristaltic action of the intestines, and thus aids in expelling flatus and overcoming constipation. When fermentative changes are a consequence of obstruction to the onward passage of the food, such as results in an extreme degree from stenosis of the pyloric orifice, our treatment is of necessity limited to relieving the distressing symptoms caused by the excess of acid, the development of sarcinæ, and the flatulent distension.

Drs Ringer and Murrell* have recently advocated the use of glycerine for the relief of flatulence and acidity. They base their recommendation on the fact that it retards some forms of fermentation and putrefaction, notably of nitrogenous substances. Experiments† show that 2 to 3 per cent. of glycerine added to milk will

* 'Lancet,' July 3, 1880.

† Dr. E. Munk, Virchow's 'Archiv,' 1879.

delay lactic acid fermentation from eighteen to twenty-four hours, and it is a well-ascertained fact that glycerine preserves meat so completely that after immersion for some months it is still fresh and can be eaten. Drs Ringer and Murrell recommend it to be taken in teaspoonful doses either immediately before, with, or directly after food. Their observations were made on stomach flatulence, and they obtained satisfactory results, for though it only partially succeeded in some cases where other remedies at once cured, in others it speedily and completely succeeded when these failed. Owing to its solubility they do not think it influences the formation of wind in the colon except when given in large doses, when it acts as a slight laxative, and so expels the putrefying mass which forms the wind. My own experience points to the conclusion that its administration is most beneficial in cases of ordinarily delayed digestion, but that it is of little value in severe cases. Glycerine, however, is an exceedingly valuable menstruum for the administration of other medicines; we can, therefore use it in all cases, obtaining the benefit it undoubtedly confers in many instances without in any way interfering with the employment of other remedies in cases where its efficacy is doubtful. Thus, bismuth may be administered before meals, pepsin during meals, and a few drops of chloroform, as an antispasmodic, after meals, in a teaspoonful of glycerine. Charcoal is useful in all cases of flatulence and acidity, and its beneficial effects are well marked in intestinal flatulence associated with offensive smelling evacuations; thus, I have employed it with considerable success in relieving the flatulence which in some cases is a very distressing symptom in chronic dysentery; it also has a marked effect in diminishing the fœtor of the stools.

Vegetable charcoal is undoubtedly more efficacious than animal, and it is best administered in a dry state in the form of powder. A convenient mode of administering it in this form is to strew a teaspoonful thickly on the centre of a slice of very thin bread and butter, then rolling this up tightly, compressing the edges to prevent the escape of the charcoal, and swallowing it with as little mastication as possible. When the flatulence chiefly occurs in the stomach the charcoal should be taken immediately before food; in intestinal flatulence immediately after.

Creasote and carbolic acid are often employed for the relief of flatulence. Dr Sansom, who has introduced the use of sulpho-carbolates, has shown that they effectually arrest fermentation; ten or fifteen grains of sulpho-carbolate of soda may be administered either immediately before or after food. Dr Ringer has pointed out that the sulpho-carbolates may be advantageously employed in cases when the patient complains of pain, often most marked on one side of the abdomen, generally the left side, under the ribs. This pain, which is temporarily relieved by the eructation of a little wind, soon returns, and may endure many hours. This pain, Dr Ringer thinks, is of neuralgic character, and is excited by flatulency.

In severe cases of flatulence and acidity I have found considerable benefit result from the use of turpentine in from ten to fifteen drop doses, taken shortly after food. By acting as a stimulant to the mucous membrane of the stomach and intestines it increases the quantity and improves the quality of the secretion, and diminishes the catarrh of those organs. It checks the formation of sarcinæ. In the majority of cases it has a laxative effect, and thus relieves constipation without recourse being

had to other remedies. The best mode of prescribing it is as follows:—Ten drops of spirits of turpentine are suspended in four drachms of acacia mixture; to this is added a drachm of glycerine, containing five drops of pure chloroform in solution, twenty grains of bicarbonate of soda, and cinnamon water to one ounce.

Opium and its alkaloids are contra-indicated in flatulent dyspepsia, since they tend to diminish the digestive secretions and the contractile movement of the stomach and intestines. Five drops of chloroform dissolved in a teaspoonful of glycerine affords considerable relief to cramp and spasm.

For the relief of acidity the alkaline bicarbonates must be administered from two to three hours after meals. Purgative medicines are to be avoided as much as possible. When absolutely required to remove accumulations, &c., dilute warm solutions of Carlsbad salts or small quantities of Fredrickshall, Pullna, or Hunyadi Janos water, should be employed in preference to drugs.

With regard to the diet of persons suffering from flatulent dyspepsia, it is important to insist on the food being well masticated before swallowed, as well as being tender, easy of digestion, and well cooked. The meals should be taken regularly, and the intervals between them not too prolonged; a weak and delicate person should take food at least every four hours. A small quantity of food should be taken on going to bed and on first rising in the morning, care, however, being taken not to overload the stomach at any one meal. With the avoidance of notoriously indigestible or flatulent articles of diet the patient need not be placed on too rigorous a dietary. Cream should be used instead of milk for tea or coffee; these, however, should be indulged in sparingly. Alcohol is borne badly by

persons suffering from this form of dyspepsia, and they are often particularly susceptible to its influence, whilst from a purely medical point of view they are distinctly better without it. In cases, however, where there is a considerable degree of atony a tablespoonful of brandy, diluted with two tablespoonfuls of water, may be given with advantage at the principal meal of the day, since *dilute* alcohol in moderate quantity is, as Bernard has shown, a very efficient stimulant of the gastric juice. Only a small quantity of fluid should by taken at meal times, and, therefore, the same benefit is not derived from the employment of "table waters" as is obtained from their use in cases of dyspepsia arising from undue secretion of acid; a small tumbler, however, of Appolinaris water taken with dinner is often of distinct service, probably from the fact of the considerable proportion of chloride of sodium it contains. Fluids are best taken about two hours after food, when they dilute the acid that may be formed, and help to remove the products of digestion from the stomach. For this purpose the natural effervescent alkaline waters may be employed. They are, however, most beneficial in cases when the flatulence is limited to the stomach, and are of little use in relieving intestinal flatulence, whilst in those cases of intestinal dyspepsia which are associated with oxaluria they are distrinctly injurious.

Flatulent patients are decidedly worse in wet, cold, and raw weather, or when they change from a dry soil to a damp situation. Those residing on wet clay soil or in marshy districts should, therefore, particularly attend to the subsoil drainage of their houses, and the use of the cold compress whenever the weather changes from fine to wet will protect them from being over-sensitive to climatic vicissitudes.

CHAPTER IV

DERANGEMENTS ASSOCIATED WITH DEPOSITS OF URIC ACID

Although, prior to the discovery of uric acid by Scheele in 1776, many physicians* taught that gout was produced by a morbific matter resulting from the "coctions" being imperfectly performed in the *primæ viæ* and in the secondary assimilating processes, still it was not till twenty years later that the probability of there being a connection between uric acid and gout was even hinted at. Indeed, at first uric acid was solely regarded as a "concreting" acid formed in the kidney, which bound together the earthy matters of the urine, and so engendered stone. This view was expressed by the term *lithic acid*—a term which is still employed clinically, though its chemical composition and relationship is best expressed by the title uric acid. In 1793, however, Mr Murray Forbes† pointed out that this substance was deposited in other parts of the body besides the urinary passages, and this, he thought, showed that it was contained in the general fluids of the body, and not merely formed in the kidneys. But though this observation was shortly afterwards confirmed

* Thomas Sydenham, 'Treatise on Gout,' 1685.

† 'Treatise upon Gravel and upon Gout, with an Examination of Austin's Theory of Stone, and Dissertation on Bile and on Solvents,' 1793.

by the analyses of Woolaston, in 1797, of gouty tophi, which he found composed of urate of soda, it was not till Dr Garrod, in 1848, brought forward before the Royal Medical and Chirurgical Society the result of his observations, based on chemical analysis of blood and urine in gout and rheumatism, that the fact that in true gout an excess of uric acid exists in the blood prior to and at the period of the attack was first demonstrated. The facts then brought forward have been since fully confirmed as to their accuracy, and although Dr Garrod does not maintain they are in themselves sufficient to explain all the phenomena of gout, still his researches have thrown considerable light on the pathology of the disease. Since Dr Garrod's observations have been published there has, however, been a tendency on the part of some writers to extend Dr Garrod's guarded statements with regard to uric acid, and they have assigned to it a place in pathology which is not yet warranted by physiological and chemical observation, nor even, I venture to think, by clinical experience. Already a reaction has set in against the doctrines enunciated by the most advanced members of this school of humoral pathology, and which, like most reactions, may in turn become extreme, and ignore many important points in connection with the pathological relations of uric acid which have been fairly established.

From the circumstance that uric acid is a di-ureide, that is, by oxidation a molecule of uric acid can be split up into a molecule of a non-nitrogenous acid and two molecules of urea, it has been assumed that when the process of oxidation is imperfectly performed within the body uric acid will be found in excess in the blood; and this assumption has been further strengthened by the

supposition that uric acid is one of the substances through which each particle of albumen passes before it is thrown out of the body. Now, whilst uric acid may fairly be spoken of as a less oxidised product of proteid metabolism than urea, yet there is no evidence, as Professor Foster* points out, to show that it is a necessary antecedent of the latter. Indeed, we have increasing evidence to show that the probable antecedents of the urea in the blood are partly the kreatin formed in muscle and elsewhere, and partly the leucin and other like bodies formed in the alimentary canal. The physiological variation, too, of the quantity of uric acid, so far as we can judge from its excretion by the urine, depends less on the nature of the food than upon special conditions of the internal organs than is the case with urea; and this also points to an origin slightly divergent from that body. Thus, Professor Parkes† found, after four days of non-nitrogenous diet, that traces of uric acid could always be found in the urine, which seems an additional argument against the origin of urea from uric acid. For why, Professor Parkes observes, when all the nitrogen was cut off, and consequently the oxygen was in relative excess, should not all the uric acid have been converted into urea if that was its usual origin in the body? It is not, however, so converted, but passes off *pari passu* with the urea as if furnished by special cells. Professor Parkes has also pointed out‡ that the comparative constancy in the amount of uric acid excreted, within narrow limits, and the want of connexion between its changes and the changes in the urea, in health and disease, seem to offer extremely

* 'Text Book of Physiology,' p. 353. Macmillan, 1878.

† 'Lancet,' vol. i, p. 722, 1874.

‡ 'Composition of the Urine,' p. 29. Churchill, 1860.

strong arguments against the supposition that the latter body is largely derived from the former. Again, the fact that in birds and reptiles uric acid replaces urea has been urged in support of the insufficient oxidation theory, since it has been urged that both have to economise oxygen — the bird for the due performance of its active vital functions, the reptile on account of the structural imperfections of the respiratory apparatus. With regard to birds, however, we have no proof whatever of their need to economise oxygen; indeed, the fact of the richness of their blood in red corpuscles points to an opposite conclusion. The final causes of the divergence in these cases Professor Forster seems to think are to be sought rather in the fact that urea is the form best adapted to a fluid, and uric acid to a solid excrement. Lastly, it must be borne in mind that uric acid and its salts are by far the most insoluble of all the organic products met with in the body, so that unless some special provision was supplied for its prompt removal, as is the case with birds and reptiles, by their voluminous kidneys, any considerable temporary excess would, especially if the excess was attributed to imperfect oxidation, lead to deposition in the textures of the body.

These considerations certainly do not give support to those who have given to uric acid an undue prominence in humoral pathology, and who have based their hypotheses on the supposition that uric acid is one of the substances through which every particle of albumen passes before it is thrown out of the body, and that when oxidation is imperfectly performed there is a production of insoluble uric acid and urates instead of urea. Indeed, they point rather to an opposite conclusion, that uric acid in the human body in health, and

even in disease, is formed in only very minute quantities, and that when it is deposited from the urine or in the tissues the fact of the occurrence of such deposit may be generally referred to its insolubility rather than to its excessive production in the system. Thus, in the majority of cases where frequent and even persistent deposits of uric acid and urates are met with in the urine, we are often unable to show that they are in absolute excess; whilst, on the other hand, it has been repeatedly demonstrated that no absolute increase does occur in a very large proportion of cases, and that the precipitation depends solely upon changes in the character of the urine, such as increase of its density or acidity, or both combined, the result of some derangement of the digestive organs, or from catarrhal or other morbid conditions of the urinary passages. Whilst in those cases in which a considerable quantity of uric acid is suddenly discharged we generally have sufficient evidence to show that the deposit has been accumulating for some time previously in the urinary passages, and does not represent the amount separated from the system within a period of twenty-four hours. Again, in those cases where an absolute increase of uric acid excreted in the twenty-four hours' urine does occur, it will be generally found on inquiry that other urinary constituents are likewise being eliminated in excess, notably the urea and phosphoric acid. The circumstances under which this elimination occurs have received but little attention; they seem to depend in many cases on disturbing influences, which apparently have a more profound origin than mere disturbance of the hepatic functions to which they are generally referred. In cases where the condition is temporary the increased elimination may often be referred to disturbance of the nitro-

genous equilibrium, induced by the employment of a too highly animalised diet, by nervous influences, or temporary disturbances in some function of the organism. These cases in their general characters correspond to the condition described by Murchison under the term *lithæmia*, though increased elimination of uric acid is not the sole urinary characteristic, nor functional derangement of the liver necessarily the sole cause of the disorder. In cases, however, where the discharge of uric acid in excess is more or less persistent in a urine of high average specific gravity, whilst the urinary secretion is not diminished in quantity, it is to be feared that the condition is a prelude to some serious organic mischief—often phthisis, and, as Prout pointed out, of uterine cancer. It is a condition which is often found preceding or alternating with saccharine diabetes, and attention has recently been drawn to the considerable increase of phosphoric acid discharged daily with the urine in these cases.* Considerable clinical importance has been attached to the fact of uric acid deposits thus alternating with sugar, as indicating an alliance of this form of diabetes with the gouty state. Without denying that such is the case in some instances, I would, however, point out that these deposits of uric acid are often more apparent than real, and depend rather on the changes in the urinary secretion itself than on any chemical transformation within the body. Thus, when sugar is abundant there is usually a corresponding increase in the quantity of water discharged, so that the relative quantity (per cent.) of uric acid is lessened ; if, however, the quantity of sugar becomes diminished, the the discharge of water from the body is generally pro-

* J. L. Tessier, 'Du Diabète Phosphatique,' Paris, 1877. Also paper by author, 'Lancet,' March 12th, 1881.

portionately reduced, whilst the acidity of the urine is relatively, if not absolutely, increased, so that the uric acid becomes relatively in excess, and is deposited partly on that account and partly from the increase in the acidity of the urine. Indeed, it is not improbable that an accumulation of acid salts in the blood may be a cause of some of the intermitting forms of diabetes; since Dr Pavy* has found that the introduction of an acid into the system produces saccharine urine, this effect has followed the injection of phosphoric acid into the general venous system and also its introduction into the intestinal canal.

There is, again, a tendency among many physicians at the present time to consider certain anomalous symptoms, which are not, however, recognised as distinct diseases, as connected with the "gouty diathesis" or due to "uric acid tendencies." Whilst admitting that these symptoms are met with frequently in patients who suffer from gout, or who are predisposed to the disease, it is important to remember that these symptoms also occur in persons in whom it is difficult by the utmost stretch of the imagination to suppose to be under the influence of the gouty diathesis, but who frequently develop at a subsequent period some other marked constitutional taint. Among the premonitory signs of scurvy are many which are also considered sure indications of the gouty state.† There are the same fugitive and erratic pains in the limbs, tenderness of the joints, attacks of dyspnœa more or less paroxysmal in character, severe attacks of pain over the region of the heart, weak and intermittent pulse, irregular discharges of urine, some-

* 'Diabetes,' p. 82.

† Sydenham, 'Opera universa,' Sect. 6, cap. 5, de Rheumatismo, 1685. Garrod 'On Gout,' p. 473, 1876.

times profuse and of low specific gravity, at other times scanty and concentrated, &c., and yet scurvy and gout are, when developed, distinct diseases.

Now, although true scurvy has almost disappeared from civil practice, and is only occasionally met with among the sailors of our mercantile marine, still, as Dr Eade* and others have shown, incompletely developed forms of it are by no means of rare occurrence, though, as Dr Buzzard† has pointed out, the true nature of the ailment is very often overlooked. Among the class of persons who form the bulk of the out-patients of our hospitals and dispensaries mild scorbutic manifestations may be frequently noted. At the London Hospital, where, from a habit acquired at the Dreadnought, I make it a rule to examine the gums of all patients at the time I examine the tongue, a visit seldom passes without a case presenting itself exhibiting sufficiently characteristic scorbutic symptoms. This manifestation of a scorbutic condition is not, however, by any means confined to our poorer patients, since we find it developing from time to time among those of a better class. Here it frequently supervenes on some chronic affection ; thus, for instance, a patient with a weak and feeble digestion is afraid of taking sugar because it turns acid, and vegetables, particularly potatoes, because they cause flatulence, so fruit, potatoes, and green vegetables are avoided. Absolute deprivation of vegetable food, however, is not required to produce a tendency to scurvy, some persons being naturally predisposed towards the disease, and are more readily and speedily affected by a temporary withdrawal or a diminished supply than others; these persons have what the older writers

* 'Lancet,' June, 1880; 'Brit. Med. Journal,' Nov. 19th, 1881.

† Reynolds' 'System of Medicine,' Article "Scurvy," p. 745.

termed the "scorbutic constitution." In many instances that have come under my observation of persons supposed to be "gouty," I have suspected them to be really suffering from an incompletely developed form of scurvy, and have noticed an almost immediate alleviation of the symptoms by recourse to lemon juice.* So also with persons who have had syphilis, but who at the time they come under observation are free from any apparent manifestations of the disease, and who often complain of symptoms that closely resemble those experienced by gouty subjects; so that if our patient's memory is short, or there are difficulties in the way of direct inquiries, we may readily fall into error. Thus, in the case of a lady who was sent to me in the spring of last year, supposed to be suffering from some "gouty trouble," her chief symptoms were periodical attacks of jaundice, though not of very severe character, followed by urticaria, with dyspnœa, irregular and weak action of the heart, shooting pains in the limbs, &c. The urine collected for the twenty-four hours showed that she passed 1520 c.c., with a specific gravity of 1029, or rather more than one half again as much solid matter as she ought. There was no albumen or sugar; urea 58·2 grammes; phosphoric acid 4·1 grammes, and the urine loaded with urates. Under a suitable dietary and alkaline treatment the quantity of urine sank to 1·100 c.c., with specific gravity of 1·021, and the excretion of urea to 33 grammes, and she felt generally more comfortable, and in three weeks was decidedly better. About this time, however, she began to complain of pain over the inner edge of the right tibia, and shortly

* When patients are fanciful, as they often are, and continue their neglect of vegetable food and refuse to take lemon juice, the latter must be prescribed for them.

after a node developed which required surgical treatment. She was then placed for a time on full doses of iodide of potassium, with decided effect on the periosteal swelling. Dr Fothergill relates* a somewhat similar case of a patient who suffered from intractable indigestion, which did not yield to ordinary treatment till a local malady, a persistent pain caused by a periosteal thickening, led to the supposition that the "underlying factor was unrecognised syphilis." Iodide of potassium relieved the pain and the indigestion. Sir James Paget has also drawn attention to the same point, in a speech made at Norwich at the meeting of the British Medical Association in 1874, when referring to the routine administration of blue-pill by the practitioners of former years, he suggested that some of the good effects attributed to its wholesale administration may have been obtained by its action on a possible syphilitic taint which had escaped the observation of the practitioner.

Again, strumous and tubercular subjects are very liable, not only to deposit uric acid and urates from their urine, but also to excrete it in excess. This is especially the case with young children, who often discharge considerable quantities of red sand, and are consequently frequent victims to uric-acid calculus.† In many cases these deposits depend solely on temporary disturbances of digestion causing a too highly acid state of the urine, but when, as is often the case, the uric acid is also found to be actually in excess and not merely deposited, whilst the specific gravity is high and the

* 'Indigestion and Biliousness,' p. 124. Lewis, 1881.

† Dr. W. Roberts, from a consideration of statistics from numerous sources, states that "the *frequency* of stone is far the greatest under five years of age, and next between ten and fifteen years. 'Urinary and Renal Diseases.'

urea also is in excess, it is generally found to precede or accompany some serious constitutional disturbance.* In adults, too, with strumous or tubercular tendencies we occasionally find patients who have for some time previously been subject to anomalous affections and pains in different parts of the body, accompanied by a more or less persistent deposit of urates or uric acid. Thus, a patient I saw this summer, who was troubled with an excessive secretion of viscid mucus in the fauces and at the back of the nose, but who in all other respects appeared healthy, except that she complained of symptoms corresponding to those so graphically described by Dr Murchison as characteristic of lithæmia; so that had I not known the family history I should probably have regarded the case as one of functional derangement of the liver. This patient's mother and a brother, however, had both died of caries of the cervical vertebræ, and another brother had undergone amputation of the thigh for disease of the knee-joint. This patient improved considerably on cod-liver oil, iron, a liberal dietary, and a brief residence at Margate—a plan of treatment which would have aggravated the symptoms had they been due to hepatic derangement. It would be possible to multiply examples, but enough has been said, I believe, to allow us to infer that many of those anomalous symptoms, the exact clinical significance of which we are not yet in a position always rightly to determine, but we are perhaps too ready to refer to as depending on a gouty condition, are not necessarily pathognomonic of that state, but may in many instances be irregular manifestations of other morbid conditions. So that excess of uric acid in the urine

* Such a condition of urine is not infrequently met with during the early stages of rickets.

should not be regarded as merely the result of defective oxidation or functional disturbance of an organ, but when that condition is more or less persistent, and is accompanied by an increase of the other solid matters of the urine, notably of the urea and phosphoric acid, it denotes an increase of tissue metabolism throughout the body, and will generally be found preceding or accompanying some grave constitutional disorder.

The clinical and pathological conditions which lead to the deposit of uric acid and its salts from the urine, or its excessive elimination from the urine, may be thus briefly summarised.

A. Deposits of uric acid or urates, not, however, necessarily eliminated in excessive quantities.

1. Absolute increase in the acidity of the urine.

The occasional deposit of urates observed in winter arises from this cause. The action of the skin being checked the acidity of the urine increases during cold weather. Similarly in many extensive cutaneous diseases, such as eczema and psoriasis, uric acid deposits are of frequent occurrence; these disorders therefore need not be attributed to lithæmia. Also in forms of dyspepsia associated with irregular secretion of gastric juice ('Acid Dyspepsia,' p. 30).

2. Relative increase in the acidity of the urine.

The deposit of urates frequently noticed during the summer months originate in this way, the cutaneous transpiration being increased in hot weather, the urine is more concentrated. Similarly in pyrexia, especially rheumatic fever, and in diarrhæa. Uric acid deposits alternating with sugar are often caused in this way; since as the sugar disappears urination is not so

profuse, and a relative increase of the acidity of the urine occurs. This relative increase may not only be caused by a diminution of the water excreted, but from deficiency of the alkaline phosphates; this condition is frequently met with in the urines of ill-nourished or strumous children.

B. Uric acid eliminated in excess, but not necessarily deposited from the urine.

1. Uric acid in excess usually attended with a diminution of the other urinary constituents (true lithæmia). Chiefly in diseases of the liver, such as acute yellow atrophy, cirrhosis, and cancer. In scurvy an excess of uric acid is generally observed, with a diminution of urea and the alkaline phosphates.

2. Uric acid in excess attended with an increase of the other urinary constituents.* In functional derangements of the liver, especially those brought about by disturbance of the "nitrogenous equilibrium" by the ingestion of too much animal food. As a condition antecedent to the development of phthisis or cancer, and sometimes of diabetes, or preceding the oubtbreak of such constitutional conditions as syphilis, scrofula, and of gout in its early attacks.

Modern theories assign to uric acid a variable *rôle* in the pathology of the gouty state. These theories may be briefly considered under three heads:—1st. Which maintains that the causes which predispose to gout are either such as produce increased formation of uric acid

* In these cases if the urinary water is increased we have a condition for which we may very properly use the term "polyuria;" when only the solid constituents are increased then the designation "baruria" should be employed. The term "baruria" was first introduced by the late Dr Fuller in describing certain forms of dyspepsia associated with excess of urea in the urine. 'Med.-Chir. Trans.,' vol. li, p. 45.

in the system, or lead to its retention in the blood, and that the causes exciting a gouty fit are those which induce a less alkaline condition of the blood, or which augment for the time the formation of uric acid, or such as temporarily check the eliminating power of the kidney, and which regards the deposited urate of soda as the cause and not the effect of the gouty inflammation.* 2nd. Which regards gout as a tropho-neurosis, and looking beyond mere chemico-pathogenetic theories, assigns to uric acid only a secondary position in relation to the production of the disease.† 3rd. The ingenious hypothesis‡ which regards gout as a mode of decay, and which does not consider the presence of urate of soda in parts of the body remote from the centre of circulation and in tissues little vascular and of low vitality as necessarily implying that uric acid is poured out to free the blood from its presence, but that rather it may be taken as an evidence of a kind of degeneration or want of tissue organisation. Views apparently so opposite are really not contradictory—for though no one of them is in itself sufficient to account for all the phenomena of gout, yet, collectively, it is possible to construct a theory that harmonises with most of the clinical phases of the disease. For instance, let us suppose the first step in the pathology of gout to be that of textural degeneration, by which the tissues and blood become loaded with effete products, that such predisposing conditions lead at last to a disturbance of some special trophic nerve centre, caused either by a degenerative change in its structure or derangement of its function by the circulation through

* Dr Garrod, 'A Treatise on Gout and Rheumatic Gout,' 3rd edition, pp. 274, 275. 1876.

† Dr D. Duckworth, 'British Medical Journal,' March 26th, 1881.

‡ Dr W. M. Ord, 'Medical Times and Gazette,' Feb., 28th, 1874.

it of impure blood. This disturbance may be considered the determining cause of the gouty attack. The result is deposition of urate of soda in the tissues, especially in those in which the specific inflammation has been excited. At present it is impossible to decide how the urate of soda is obtained to form the deposit. It may be derived—

(*a*) From the blood, by an excessive formation, or, as Dr Garrod suggests, by an accumulation, owing to diminished excretion by the kidney. The latter supposition is highly probable since, the nervous disturbance that determines the attack may at the same time disorder the renal function so far as the excretion of uric acid is concerned.

(*b*) The specific inflammation may cause increased formation of uric acid in the affected tissues.

(*c*) Or with, or without, increased formation, chemical or vital changes may take place in the tissues themselves, which lead to the deposition of the urates formed in them, which under normal circumstances would be removed into the general circulation.

But the question which is of the first importance to determine is the nature of the predisposing causes that lead up to the gouty seizure, since this problem must necessarily be solved before we can proceed to discuss the nature of the conditions which the actual attack brings before us. The subject can only be fairly considered with respect to subjects in whom gout is acquired, since those in whom the disease is hereditary have already acquired the "constitutional aptitude," and the earliest alterations that take place in tissue and function are at present beyond our power of investigation. When, however, the disease is acquired, several abnormal physiological conditions lead up to and are

antecedent of the pathological state. What effect these altered conditions have in bringing about primary changes in the chemical quality of the blood which may be supposed to be concerned in the production of the disease, and what the nature of those changes are, we will now consider.

It has been already observed that the premonitory symptoms of scurvy closely resemble those that generally precede an attack of gout. There are the same fugitive and erratic pains in the limbs, tenderness of the joints, attacks of dyspnœa, &c. Indeed the close resemblance between gout, rheumatism, and scurvy in early stages of the disease has repeatedly attracted the notice of writers on the subject since the time of Sydenham, who first drew attention to this point.* Now, no fact in medicine is perhaps more clearly established than that the exclusive cause of scurvy is the prolonged and complete withdrawal of succulent fruits and vegetables from the dietary of those affected—the very articles of food concerned in supplying the blood with the alkaline carbonates to maintain its alkalinity. To Dr Garrod† belongs the credit of suggesting that the cause of the disease lay in the diminution or withdrawal of one of the alkaline constituents of the blood, since in 1848 he made the observation that in scorbutic diets potash existed in smaller quantities than in antiscorbutic ones, and was led from that circumstance to determine the amount of that substance in the blood and urine of a patient

* "Thus," he says, "for instance, where matter suited to produce the gout is newly generated there appear various symptoms which occasion us to suspect the scurvy, till the formation and actual appearance of the gout remove all doubt concerning the distemper."—'De Rheumatismo,' Sect. 6, cap. 5.

† "Nature, Causes, and Prevention of Scurvy," 'Edinburgh Monthly Journal of Medicine,' New Series, vol. ii, p. 457.

suffering from scurvy, and he found it considerably diminished; and from this observation he brought forward a theory that scurvy depended upon a deficiency of this alkaline oxide in the system. The result of some analyses* I have made confirm the fact observed by Dr Garrod, that potash is diminished in the urine of patients suffering from scurvy, and I have further shown that in order to maintain the proper degree of alkalescence of the blood, the alkaline phosphates are retained in the system, and consequently become diminished in the urine, although the quantity ingested was the same. The primary change, then, in scurvy appears to be a chemical alteration in the quality of the blood in the direction of diminished alkalinity. In gout a diminution of the alkaline reaction of the blood has been observed, and Dr Garrod† has pointed out that, "with the exception of collapsed cholera and perhaps certain cases of albuminuria, the reaction of the blood is found to be nearer the neutral point in severe forms of chronic gout than in any other disease." This diminished alkalinity of the blood in the case of gout has manifestly a different origin than what happens in scurvy; there, as we have seen, it is the result of the withdrawal of alkaline salts supplied by fresh vegetables and fruits. In gout the diminution is caused by the positive addition of acid and acid salts, either taken in excess with the food and drink or retained in the system, the result of imperfect elimination, in consequence of sedentary habits or the action of certain metallic poisons.

Our views with regard to the nature of the acids con-

* 'Inquiry into the Pathology of Scurvy.' By the Author. Lewis, 1877.

† 'Reynolds' System of Medicine,' article "Gout," vol. i, p. 826.

cerned in the production of gout have been limited in recent years solely to a consideration of the conditions which lead to an increase of uric acid in the system. Yet clinical experience does not altogether support this exclusive view. For if the acids concerned in the production of gout were derived solely from the nitrogenous elements of the food and tissues, then by a rigid limitation of animal food within physiological limits we might hope to check or control the progress of the disease. But gouty patients complain that other articles of diet besides the nitrogenous, or those, which like alcohol, disturb the function of the liver, and are thus supposed to lead to increased formation of uric acid, give them arthritic trouble; and they will affirm there is as much gout in a plateful of apple tart as in a mutton chop, and in a few strawberries as in a glass of port wine.

It is probable, therefore, the influence that an excessive animal diet has in the production of the gouty state is not due so much, though it is in part, to the actual introduction of acid into the system, either by the small quantity of acid sodium phosphate that exists in the juice of flesh, or from the increased manufacture of uric acid, but to the increased tissue metabolism that it induces throughout the body, and which, when continued for any length of time, leads to degenerative changes.

With regard to the habitual and excessive use of alcoholic beverages and their effect on the production of gout, although undoubtedly they cause more or less derangement of the liver, I do not hold, as I believe many do, that this derangement leads to increased formation of uric acid (at all events it has not been positively proved that it does so), for if that were the case, then the higher the alcoholic value of the beverage

the greater would be the tendency to the formation of uric acid; yet it is not the spirit drinkers who suffer from gout. The fact is, I believe, that all alcoholic beverages contain free acids, acid salts, and saccharine material, and that these are the deleterious elements, the wines containing the most of these being the most decidedly gouty. Thus we find of the wines in ordinary use, port and sherry, are most rich in saccharine matters, and Burgundy in acids and acid salts, but which contains more sugar than the lighter acid wines, claret and hock. Spirits, with the exception of "sweetened" or London gin, which has a reputation of being provocative of gouty seizures, are nearly altogether free from these substances. But beers, especially London porter, contain as much at 1·2 oz. of sugar and dextrin, and 25 grains of free acid in each pint. Thus the lightermen who unload the colliers in the Thames are, as Dr. Budd pointed out some years ago, great sufferers from gout, and are great consumers of porter, often drinking a gallon of this fluid over one job, and are, therefore, instances of the development of the disease under the influence of a mild alcoholic drink, but which is rich in sugar and free acid.* It is the sugar introduced with the food and

* The following table, which gives the absolute amount of alcohol, free acid, and sugar in a gallon of London porter, port-wine, claret, gin, and whiskey respectively, shows what an acid and saccharine mixture porter really is.

Constituents in 1 *gallon.*

	Alcohol.	Free acidity.	Sugar.
London porter . .	7·5 oz.	4000 grains.	9·8 oz.
Port wine . . .	30·0 oz.	480 grains.	5·2 oz.
Claret (medium) .	18·5 oz.	820 grains.	0·4 oz.
Gin (London) . .	75·0 oz.	32 grains.	1·2 oz.
Whiskey . . .	75·0 oz.	32 grains.	Traces.

drink that furnishes most of the acid developed in the body, and it is, therefore, the saccharine rather than the nitrogenous elements of the diet that require restriction. Sugar, by fermentation in the intestinal canal, yields lactic acid, and this when absorbed into the blood is reduced to carbonic acid. When the quantity introduced is not excessive, this carbonic acid unites with the alkaline bases, soda and potash, in proportion to form normal carbonates (Na_2HCo_3), one atom of acid to two of alkali, but when a considerable quantity is poured into the circulation the amount of alkaline bases are probably insufficient to furnish two atoms of base, but only one, to combine with the carbonic acid, so we have instead the acid (bi-) carbonate (NaH_2Co_3), an acid salt with an alkaline reaction, but which I have shown (p. 11) is capable by decomposition with neutral salts of forming acid salts with acid reactions.*

Sedentary habits, especially when food is taken in excess, undoubtedly lead to the accumulation of acid in the system. Professor Parkes, in his work on 'Hygiene,'† has given a concise table showing the effect exercise has on the absorption of oxygen and the

* It is probable the reason some fruits, such as strawberries, and fruit tarts, provoke arthritic pains in the gouty is that the saccharine element taken with them predominates over the alkaline bases contained in the fruit, and the salts enter the system as acid salts rather than alkaline. In the typical antiscorbutic fruits and vegetables (lemons, cress, and cabbage) alkaline bases abound, and the salts derived from them no doubt enter the system as normal not acid carbonates, thus helping the serum of the blood to regain its proper degree of alkalinity.

† 'Practical Hygiene.' By Ed. A. Parkes, M.D., F.R.S., late Professor of Military Hygiene in the Army Medical School, Netley. Fifth edition, by Prof. du Chaumont, Professor of Military Hygiene in Army Med. School, Netley, p. 411. London: Churchill, 1878.

evolution of carbonic acid, which shows that on a "work day" 8½ oz. of oxygen were absorbed in excess of a "rest day." And that 13 oz. in excess of carbonic acid were evolved on the "work day," although the so-called "work day" included a period of rest, the work being done only during working hours, and was not excessive. The accumulation of carbonic acid in the blood would, as I have already explained, increase the acid salts present in the blood, since the free carbonic acid would take a portion of the base from the normal carbonates (Na_2HCo_3) to form acid carbonates (NaH_2Co_3). Over-fatigue from excessive muscular exertion may also lead to an accumulation of acid in the system, owing to the want of a sufficient supply being brought to them to burn the carbon elements which supply their force, and also from the accumulation of the products of their combustion. Exhaustion of the nervous system from overwork probably acts in the same way, a condition of general fatigue being induced, which, acting through the nervous system on the heart and visceral organs, causes the blood to circulate less vigorously, and the process of renewal and removal to become slacker and slacker.

Lastly, the acceptance of the view that the first step in the production of gout is due to some chemical alteration in the quality of the blood, chiefly in the direction of diminished alkalinity, will do much to establish the pathological relationship between scurvy, rheumatism, and gout, a relationship that has long been held by many to be possible.* Thus, scurvy is induced by a

* Mr Jonathan Hutchinson, in a paper read before the British Medical Association at Ryde, enunciated a series of propositions, clearly showing the relationship, as well as the points of distinction, between gout and rheumatism, 'Brit. Med. Journal,' Aug. 27, 1881.

diminished alkalinity of the blood owing to the withdrawal of alkaline bases supplied by vegetable food; the disease may be considered as an instance of the acute effect of "acid" on the tissues generally, the appearance of positive symptoms being rarely delayed more than a few weeks after the complete withdrawal of vegetable food. Owing to this rapid development, the textural degenerations met with in this disease are marked, resembling those that occur in animals when attempts have been made to reduce the alkalinity of the blood or to neutralise it, viz. dissolution of the blood globules, ecchymoses in the heart, blood stains in the mediastinum, gums, and mucous surfaces, with fatty changes in the muscles generally and in the secreting cells of the liver and kidney. In gout the diminished alkalinity is induced by the positive addition and accumulation of acid and acid salts in the blood. The process is a gradual one, and consequently the degenerative changes are not of the same acute character, and are limited to parts remote from the centre of circulation and in tissues little vascular and of low vitality. As a consequence, inflammation is readily excited in these tissues, leading to a deposition of urate of soda. This deposit may arise either from the specific inflammation causing increased formation of uric acid in the affected tissues, or, with or without increased formation, chemical and vital changes may take place in the tissues themselves, which lead to the deposition of the urates formed in them, which under normal circumstances would be removed into the general circulation. Associated with this impairment of tissue, there is a disturbance of in-

See also Trousseau's observations on the parallelism between gout and rheumatism, 'Clin. Lectures,' vol. iv, p. 386, Syd. Soc. Trans.

nervation, which in a minor degree gives rise to certain "anomalous symptoms," and which in a higher degree determines probably an actual attack of gout. In rheumatism there is also an abundant development of acid, but it is local rather than general, and is excited by catarrhal influences rather than by previous accumulation of acid in the tissues and fluids. The acute manifestation of the disease occurring for the most part among young adults, or during the earlier period of middle age, there is not the same impairment of tissue, which may probably account for the non-deposition of urate of soda, or else the specific character of the inflammation being excited by a different cause, and not to a prolonged saturation of the tissues with acid products, does not lead to the formation of uric acid in excess in the tissues.

With regard to the treatment of the derangements which are usually associated with deposits of uric acid, our course will be influenced necessarily by the opinion we have formed regarding the origin and relationship of this body in the system. If we hold with the view that considers it to be one of those substances through which every particle of albumen passes before it is thrown out of the body, and that when oxidation is imperfectly performed there is an over-production of uric acid instead of urea, and that the excess of uric acid in the blood (*lithæmia*) gives rise to disturbances of health and function, then our efforts will be directed mainly to the promotion of oxidation within the body, and limiting as far as possible the use of food rich in albuminous constituents. If, on the other hand, we believe, and as I have endeavoured to show we have reason to do, that uric acid in the human body in health, and even in disease, is formed in only minute quantities, and that when

it is deposited the fact of the occurrence of such deposit may be generally referred to its insolubility than to its excessive production in the system, our attention will then be primarily engaged in the discovery of the circumstances which bring about the deposit of this insoluble substance, and our subsequent efforts engaged in their removal and in remedying the inconveniences caused by its local accumulation and deposit. In short, if this view be accepted, uric acid will be regarded as a consequence and not a cause of the manifold disorders to which it has been said to give rise. What the conditions are which lead to the deposition and excessive elimination of this substance have been fully considered, and a concise summary given (pp. 77). From a consideration of these it will be seen how varied our treatment must be if we wish successfully to deal with this manifestation of disordered action within the system. And in order to do this the urine must be completely and thoroughly examined, not merely with reference to the absence and presence of deposits of uric acid and urates, but with regard to its quantity, its actual acidity, and the amount of solid matter passed daily. It is by this means alone that we can get an insight into the nature of the metabolic changes occurring within the body. Whilst a more or less persistent tendency to deposit urates or uric acid should lead to a careful and frequent examination of every organ of the body, and a close inquiry into the personal and family history of the patient. Believing, as I do, that these deposits are among the earliest indications afforded of disturbances abnormally affecting tissue metabolism within the body, I cannot too earnestly insist upon this point. Unfortunately the fact that these deposits are so frequently dependent on some slight disturbance of digestion has

lessened their value in the eyes of medical practitioners as a clinical indication of importance. It should not be forgotten, however, that deposits resulting from gastric and hepatic derangement speedily disappear under appropriate treatment, whilst those dependent upon general constitutional disturbance are unusually obstinate and persistent, and associated with an increase* of the other urinary constituents. It is only, however, by paying attention to these details in their minutest particulars that we gain any clue into the conditions which are leading to this manifestation, and from an attentive consideration of them we shall learn how it is that some yield to treatment by acids, others to alkalies, whilst another group of cases are benefited by tonics, iron, arsenic, quinine, and cod-liver oil, others by blue pill and saline aperients, and some, and those not a few or exceptional, by antisyphilitic treatment, although there may be no outward manifestation of the disease, and we are only guided to our conclusion by the confession of the patient.

In conclusion, it remains to say a few words with regard to the treatment of gout, and here again we are confronted with opposed opinions and diverse theories. We have two extreme schools to discriminate between,

* My friend, Dr Andrew Duncan, drew my attention to a remarkable instance of this, occurring in one of my patients at the Seamen's Hospital during the period he was house physician there. An old man, with some nervous affection of syphilitic origin, was passing a very considerable amount of urine of high specific gravity, which deposited red sand in abundance. He was taking a mixture of iodide of potassium and bicarbonate of potassium, and the latter salt was increased till three drachms daily were given, with a view of rendering the urine alkaline. This it never quite succeeded in effecting, and the character of the urine remained unaltered till an improvement in the patient's general health took place.

those who may be termed the ascetics and those who advocate the tonic treatment of the disease. Intermediate between these are a few who are content to follow the rules laid down by Sydenham, who, whilst advocating temperance both in food and drink, pointed out the danger of a too great abstinence, and who, whilst allowing that wine might prove injurious as an ordinary beverage, thought more danger arose from the exclusive use of water. The practice of the ascetic school is based upon the assumption that gout occurs from an over-production and accumulation of uric acid in the system, arises in part from a too free indulgence in the albuminous constituents of the food, and in part from defective oxidation within the body, in which, according to their views, the liver is largely concerned. Hence they rigidly limit the amount of animal food and forbid alcoholic beverages for fear of disturbing the function of the liver. As, however, I have already stated, it is not the albuminous constituents of the food that gouty persons chiefly complain of as exciting their gouty troubles, but the saccharine, whilst it is not the beverages containing the most alcohol that are provocative of gout, but those which are most rich in sugar, considerations which make it probable that the non-nitrogenous acids play a part of equal, if not of more, importance in the pathogeny of gout than uric acid. The ascetic plan of treatment is no doubt a wholesome discipline for those who, by indulgence in the pleasures of the table, are on the high road to acquiring the disease; but to those individuals with feeble constitutions, the inheritors of gouty troubles, or those who are already weakened by repeated attacks of the disorder, too great abstinence undoubtedly increases the debility and aggravates the malady. The advocates of the tonic plan of treatment hold nearly the

same views with regard to the connection between gout and uric acid as those held by the ascetic school, but instead of endeavouring to combat the formation of uric acid they aim at promoting its elimination. Of the two they do infinitely less harm than their opponents, for a generous diet within reasonable limits is undoubtedly distinctly beneficial to those suffering from atonic gout, or those in whom the gouty paroxysms are frequent but imperfectly developed, a class of cases far more numerous in the present day than those of sthenic or frank gout. But whilst generous the diet must be sparing, or else the blood, already overcharged with effete products, and the tissues themselves undergoing but slowly their transformation changes, the food thus taken in is not assimilated, and adds to the trouble of the already burthened body. In short, in order to hit the golden mean we must recur to the rules laid down by Sydenham two centuries ago for the dietetic and hygiene management of the gouty patient.

In the first place the food must be easy of digestion and should be as varied as possible. Fish should be the chief article of animal diet; white meat such as poultry and lamb, veal and pork excepted, should be preferred to red meats. When these are partaken of, it is as well to remember that the neck cutlets of mutton and the fillet of beef are more juicy and tender than the loin chop or rump steak. All roast meats should be cooked with the gravy retained in them. Bread should be eaten stale, better as toast. Potatoes, except in the form of "chips," and those only in small quantity, are to be avoided, so also all flatulent vegetables—cabbage, spinach, onions, turnips and peas; in their place simple salads should be freely partaken of. Tomatoes cooked in various ways, the soft white flower of the spring broc-

coli, french beans, stewed celery, seakale, lava, may all be used. Watercress should be served at every meal. Sweet fruits and cooked fruits, with added sugar, must be forbidden. But the subacid fruits may be employed in moderation, but even these may occasion heartburn and acidity, and give rise to cramp. Pastry, on account of its richness and the sugar it contains, should be abstained from, but plain rice, bread-and-butter, and custard puddings, with but little sugar, may be eaten each day at dinner with advantage. Savoury omelettes, caviare, olives, &c., need not be forbidden if partaken of in moderation. With regard to the use of alcohol, the special requirements of each patient must be taken into consideration. It should be taken in as dilute a form as possible, and the beverage selected must also be comparatively free from sugar. It is impossible to decide what wine will suit a gouty patient best. It often happens, as Dr Prout remarked many years ago, that those individuals who have long been accustomed to the use of the stronger wines, as port and sherry, or who have been drinkers of ale, often suffer from pains in back and gravel when they are first placed upon light wines, such as claret, hock, and champagnes, and this is especially noticeable in cold weather. It is, therefore, as well to make no sudden change, especially with elderly people, beyond reducing the quantity and substituting a dry and lighter port or sherry if the taste had previously been towards a fuller and more bodied wine. When, however, the light wines can be taken without occasioning gravel or pains in the back, the superior growths of the light clarets, such as St. Julien and St. Estephe, are preferable to clarets of the higher class, such as La Rose or Lafitte. Zeltinger, a still Moselle, is also a wine that gouty persons as a rule are able to take

without discomfort. All wines should be drank directly from the cask or after they have been bottled some time. Newly bottled wines are most pernicious. Alcoholic beverages should only be indulged in once during the day, and should then be taken with the principal meal. As the digestive powers are usually enfeebled in persons who have suffered long from gout a little *dilute* alcohol, which, as Claude Bernard has shown is, next to the saliva, the most efficient agent in stimulating the gastric secretion, should be taken at the commencement of dinner. The best form is a tablespoonful of brandy in half a tumbler of water, or a spoonful of sherry in the soup. No other alcohol should be taken during dinner, but afterwards a couple of claret glasses of some light wine or two small glasses of dry port or dry sherry. If the patient is very weak and the nights are sleepless a little brandy or whiskey may be permitted before going to bed; this is best taken in some natural alkaline effervescing water.

The meal hours should be regular. The fast should be broken immediately on rising before the fatigues of the toilette. Then a light breakfast, consisting of a poached egg, or a rasher of bacon, or a little fresh fish. Tea is preferred to coffee or cocoa, which are apt to disagree. Gouty individuals should endeavour to acquire a taste for taking this beverage without milk or sugar; after these substances have been disused a short time their addition becomes positively distasteful. Lunch should be a light meal—a basin of clear soup, vermicelli, julienne, or croute aux pôt, a few sandwiches, or a slice of cold meat with salad. Dinner should not be too late, certainly not later than seven, and three good hours should be allowed to intervene between the completion of the meal and the hour for retiring to rest.

Gouty persons are extremely susceptible of fatigue, and though exercise is necessary for them as it is for all, the amount taken should be carefully regulated. The best form of exercise is that which can be taken on horseback, next driving, walking about three or four miles daily, if it does not bring on arthritic pains in the limbs. Bathing is an exercise which the gouty should employ freely. The bath should be taken tepid (78° F. to 85° F.), since hot baths enervate and cold baths depress the system too much. Sea water or a solution of sea salt is beneficial, and the pleasantest form is as a douche. After the bath the limbs should be gently rubbed by an attendant with a soft towel, and then if the muscles are at all wasted from disuse of the limbs they may be gently galvanised. Late hours are to be avoided and crowded assemblies. The passions both of the body and mind should be kept in control.

With regard to the medical treatment of gout. When gout develops in a frank form the almost universal consensus of opinion is in favour of non-interference. The pain should be soothed by simple anodyne fomentations, or if very severe by the internal administration of opium, or by the subcutaneous injection of morphia. When, as it often happens, after a sharp attack of frank gout has subsided, the patient continues to be troubled with minor manifestations of the disorder, and the joints continue painful and slightly swollen, we are often called upon to relieve the patient and employ specific remedies. For this purpose colchicum is the drug generally employed. I have, however, a strong objection to the use of this medicine, and since the introduction of the salicylates I have had no occasion to employ it, except in a few cases where patients have already become so habituated to its use that they

profess themselves unable to do without it. Under these circumstances it is better to prescribe the drug, and so regulate its use, than allow the patient to physic himself indiscriminately with quack preparations. I have never found, however, the salicylates to fail in relieving these harassing attacks, and their effect is most marked in those patients who have not habituated themselves to the use of colchicum. Strapping or bandaging the joint is also useful in relieving the pain and swelling when it continues after the subsidence of the acute attack, acting no doubt beneficially in causing contraction of the relaxed vessels round the joint. Between the attacks the patient should attend to his general health and strictly follow the regimen I have indicated. He will require no special medical treatment beyond the means taken to ensure a daily and sufficient evacuation of the bowels. The aperients selected for this purpose should be of the mildest character, The best, when the meal hours are regular, is a little rhubarb combined with ipecacuanha, nux vomica, and belladonna, in the form of a pill, to be taken half an hour before dinner, or a drachm or a drachm and a half of Rochelle salt, with twenty grains of bicarbonate of soda and an ounce of decoction of aloes, taken before breakfast is an agreeable aperient. If the patient becomes sallow and the skin harsh and dry, and the motions light-coloured, a small dose of sulphate of magnesia should be given. In the so-called atonic gout benefit will be derived from alkaline ferruginous preparations given in minute quantities (one grain of ammonio-citrate or iodide of iron three times a day). If the pharmaceutical preparations of iron are not borne by the stomach then recourse must be had to the natural chalybeate springs of Spa and Pyrmont on the Continent

and Bath in England. In chronic gout the patient is hardly ever free from some manifestation of the disorder, whilst the paroxysms of the disease if not so severe are more prolonged and more joints are implicated than when the attack is perfectly frank. It is when gout assumes the chronic form that the crippling effects of the disease become formidable. It is in these cases that the physician is called upon to exercise all his perseverance and ingenuity. The sufferings of the patient are so constant, and the danger of visceral complications arising are so imminent, that the medical attendant has to be ever on the alert either to relieve immediate symptoms or to ward off those impending. Added to this, the crippled state of the patient by preventing the proper amount of exercise being taken the digestive functions become greatly disordered and troubles of the lower bowel supervene, whilst the patient is fortunate if the case is not complicated with gravel, so that renal and vesical sufferings are not added to his misfortunes. When all these circumstances are considered it is really surprising the ages these patients will sometimes attain.* The treatment of these cases must be based on general principles, since any special line of treatment is sure in the long run to do more harm than good. It is often difficult to resist the appeal of the suffering patient to be allowed to try some far-famed specific or even an open dose of colchicum, but permission is fraught with danger, since visceral complications are very liable to be excited by them, a sad instance of which came

* A patient of mine recently died at the age of eighty-two, who had suffered from gout and calculous disease of the kidney for forty-three years. She survived, however, four of the physicians who attended her in succession, viz. Dr Prout, Sir James Clark, Dr Brinton, and Dr Bence Jones.

under my observation quite recently. A gentleman, aged sixty-six, who had suffered from periodic attacks of gout for some years, but which had lately become more frequent, the urine at the same time containing traces of albumen, had been warned against the use of colchicum or quack medicines containing colchicum, found one night his foot unusually painful, and fearing that an attack of gout was supervening which would prevent his attending a business appointment during the week, took without consulting his medical attendant a whole box of "gout pills." The joint attack subsided, but the patient became so seriously ill that a medical man had to be sent for, who found the patient had acute nephritis, the urine loaded with albumen; œdema of the lungs rapidly supervened, and the patient not many hours after he was first seen by a medical man died.

There is one drug, however, which if judiciously administered and carefully watched is of the greatest service in the treatment of chronic gout. Paracelsus was the first to employ opium in the treatment of gout, and it was his successful treatment of a rich prelate of the church, Canon Lichtenfelds, for this disease with this drug that led to his being appointed Professor of Medicine to the University of Basle. Sydenham was loud in his praises of this remedy for the relief and control of the disease. Of late years, however, the practice of giving opium for the treatment of gout, otherwise than for the relief of pain, has declined. This no doubt is owing to our being more alive to the danger of an overdose proving fatal if there is any kidney complication than our predecessors. When, however, there is no evidence of renal complication we may give opium. Under its use the patient suffering from chronic gouty troubles makes a definite improvement. The attacks of pain in the joints become

less frequent and less severe, the patient is not so restless, fretful, and irritable, and the digestive functions often improve in a remarkable manner. It is as well, however, to combine some portion of the opium with an aperient. I therefore generally prescribe two sets of pills, those to be taken at night combined with a little colocynth or rhubarb, and those which consist simply of half-grain doses of compound soap pill (one-tenth grain of opium) combined with a little nux vomica, or any other medicine I may desire to give with it, for use in the daytime.

CHAPTER V

DERANGEMENTS ASSOCIATED WITH DEPOSITS OF OXALATE OF LIME

THERE are few subjects in urinary pathology which have excited keener controversy than that which concerns the causes tending to produce a deposit of oxalate of lime crystals in urine. Originally discovered by Wollaston in 1803 as the constituent of the mulberry variety of calculus, its presence as a crystalline deposit in the urine was for a long time overlooked. In 1842 Dr Golding Bird, in the 'Medical Gazette,' drew attention to the fact that oxalate of lime was frequently present as a crystalline deposit in urine, and detailed a series of nervous and dyspeptic symptoms which he alleged were associated with the appearance of this salt in the urine, and which he supposed to be intimately connected with an increased production of oxalic acid in the system. Dr Golding Bird's observations were at first accepted with some degree of hesitation, but subsequently they received the support of Beneke* and Begbie.† As more extended observations were made it was found that crystals of oxalate of lime were of very frequent occurrence, that they were found in urine under a variety of patho-

* 'Zur Phys. und Path. des Phosphors und Oxalsaure Kalkes,' 1850. 'Zur Entwicklungsgeschichte der Oxalurie,' 1852.

† 'Edinburgh Monthly Journal of Medicine,' March, 1848.

logical conditions, that they were so far from being invariably associated with a train of nervous and dyspeptic symptoms that they were frequently met with in the urine of persons apparently enjoying robust health. Hereupon a reaction ensued, and the opinion gained ground that these deposits had no clinical significance whatever, and it was even called in question whether the oxalic acid found in the urine ever existed in or was excreted as such from the blood, and it was suggested that oxalic acid was merely a product produced by changes occurring in the urine after emission. In England these views have been advocated by Basham,* Bence Jones,† and Owen Rees.‡ The latter gentleman goes so far as to regard "oxalate of lime merely as uric acid, or urate altered after secretion," and states that he has entirely failed to detect the peculiar pathological conditions which have been said to connect themselves with the so-called oxalic acid diathesis, and is convinced that it must be regarded as an accidental and unimportant modification of that most significant variation from health which consists in the excretion of uric acid, or its compounds, in abnormally increased proportion. This relegation of crystalline deposits of calcium oxalate to a position of almost absolute insignificance, except with regard to the question of the formation of calculi, has received very general acceptance with the profession. Facts, however, are now known which point to the conclusion that oxalic acid is formed in the organism and excreted with the urine, and that uric acid, though it may be a factor, is not the only source from which it is

* 'Renal Diseases,' p. 187, 1870.

† 'Lectures on the Application of Chemistry to Pathology and Therapeutics,' p. 98, 1867.

‡ 'Croonian Lectures,' pp. 22, 99, 1856.

derived, either by oxidation within the system or by decomposition after it has been excreted.

Whoever has been in the habit of making frequent observations as to the character of urinary deposits will have noticed that crystals of oxalate of lime occur most frequently in two distinct classes of urines. The one of deep yellow or orange colour, of high specific gravity, usually containing an excess of urea and phosphoric acid, and turbid with mucus and urates; the other pale, of a citron-yellow, or greenish hue, of medium specific gravity, and perfectly clear except at the bottom of the urine glass, where a slight cloud of mucus is collected, and in which deposited oxalates will be found. In the first instance, which is the one most frequently met with, the oxalate of lime may probably be occasionally formed in the urine, subsequent to emission, from chemical changes taking place in that fluid, especially if it has been kept some time, such as decomposition of uric acid and urates, or by the oxidation of the pigmentary matters and mucus (acid fermentation). In the latter case, which is less frequently observed, there is very little reason to doubt that the oxalic acid comes from the blood, as I hope presently to show. Again, urines such as are described under the first category are met with under a variety of pathological conditions—frequently during the course of most febrile diseases, in pulmonary and cardiac affections, in which respiration is impeded, and in disorders of the hepatic functions. In these cases, however, the presence of oxalate of lime crystals is by no means constant; sometimes appearing and disappearing without any apparent reason or alteration in the general condition of the patient; and, lastly, if these urines be filtered shortly after emission, whilst still warm, a considerable crop of oxalate of lime crystals

will subsequently form. On the other hand, in the second variety, filtration after emission greatly checks the tendency to subsequent formation of oxalate of lime crystals, though there is an abundant deposit from a sample of the same unfiltered. Unlike the other form, the urinary phenomena are usually very persistent, and the same character of urine is met with day after day, whilst with it is associated a form of dyspepsia inducing considerable emaciation and attended with intense nervous depression and hypochondriasis. Had these clinical distinctions been insisted on at first, a discrepancy of opinion would, perhaps, never have arisen. Unfortunately Dr Golding Bird and his supporters, finding oxalate of lime associated in some of their cases with a train of distinct and peculiar symptoms, regarded the appearance of these crystals in the urine in every instance as having a far more extensive pathological significance than they really had. On the other hand, Dr Owen Rees and those who advocated his views, remarking the numberless instances in which oxalate of lime deposits are met with in the urine without being able to connect them with any special pathological conditions, overlooked or disregarded the cases in which these exceptional conditions had been noted by other observers, and thus came to regard these deposits as accidental and unimportant, and indicating nothing more than uric acid, or urates altered after secretion.

The view that oxalate of lime in urine was derived from the decomposition of uric acid was based on the hypothesis that uric acid contains the elements of oxalic acid, carbonate of ammonia, hydrocyanic acid, and formic acid, and that the decomposition could be effected by simply heating the urine. The decomposition of uric acid, however, is not such a simple matter as is

here represented. Indeed, the stability of uric acid under treatment has suggested a doubt to chemists whether it contains *preformed* residues of urea, since in all undoubtedly so constituted bodies the residues of urea are removable or decomposable with the greatest facility. Nevertheless, a molecule of uric acid under the action of powerful oxidising agents does yield two molecules of urea and one molecule of a carbon acid of *some kind or other*, according to the nature of the agent employed. Thus with acids uric acid first breaks up into alloxan and one molecule of urea, and alloxan by hydration yields mesoxalic acid and another molecule of urea, and the mesoxalic acid by oxidation yields carbonic acid and oxalic acid. By oxidation with alkalies uric acid is first converted into allantoin and carbonic acid; then the allantoin by hydration becomes urea and allanturic acid, and allanturic acid by oxidation yields urea and glyoxylic acid.* Now, within the body, under the influence of increased oxidation, it is possible that these decompositions may occur. But, as a considerable quantity of oxygen is required to effect the reductions, and as the clinical and pathological conditions in which we meet with oxalate of lime in the urine do not point to increased oxidation going on within the body, but the reverse,† the occasions in which it can be derived

* For more complete details refer to Professor Foster's 'Text-Book of Physiology,' p. 615; or Professor Odling's 'Lectures on Animal Chemistry,' pp. 129—140.

† There is great confusion on this point. Thus Murchison, in his 'Croonian Lectures on Functional Derangement of the Liver,' after remarking that "Sehmidt and other chemists state that within the body oxalic acid is formed by the *oxidation* of lithic acid," in the next sentence observes, "When lithic acid is *imperfectly oxidised* it is believed to break up into urea and oxalic acid." Dr Bence Jones ('Lectures on Pathology and Therapeutics,' p. 95)

from this source must be rare and exceptional. Uric acid, too, after it is voided in the urine may possibly undergo decomposition, but it can hardly be supposed that such a stable body undergoes spontaneous change without some powerful oxidising agencies being at work to produce the result, yet in typical cases of oxaluria we frequently discover crystals of oxalate of lime as soon as they have had time to settle and collect, and yet have no evidence that any change has taken place in the urine since its emission. Again, if uric acid by its decomposition yields oxalic acid so readily, we should expect to find it rapidly disappearing as the process went on; but we have no evidence that this is the case, or at all events till some considerable time has elapsed. Again, with reference to Dr Owen Rees's assertion that if urine loaded with urates be heated, and then allowed to cool, oxalate of lime will, after the space of a few hours, be found in abundance, though none may have been detected before. This observation, however, has been questioned by Parkes,* Racle, and Neubauer,† but still, admitting it to be correct, it is sufficient to remark that the application of heat materially assists oxidation, and as oxalate of lime frequently occurs in freshly passed urine, when there is no deposit of urates and heat is not applied, and there is no evidence of any change having taken place in the urine itself to account

also makes the statement, "When uric acid is *imperfectly oxidised* it divides into oxalic acid and urea." From the decompositions of uric acid which I have given above, it will be seen that the *imperfectly oxidised* products are alloxan, urea, and mesoxalic acid, whilst oxalic acid is only obtained by oxidation being carried to its ultimate stage.

* Op. cit., p. 224.

† Liebig's 'Annalen,' Band cvi, p. 59. 'Archives des Vereins,' Band iv, p. 7.

for the formation of the crystals, it has but little bearing on the question.

From a consideration of the foregoing, I think the conclusion may fairly be arrived at that the conditions under which oxalic acid is formed from uric acid in the system are extremely limited and exceptional. If oxalic acid is formed directly from uric acid within the system, it must be under conditions which promote increased oxidation within the body—such, for instance, as pure air, exercise, sea-bathing, &c.—conditions which, it need hardly be said, are generally resorted to for its removal. In the second place, without denying the possibility of oxalic acid being ultimately formed in urines from the decomposition of uric acid, I think we may affirm that no deposit of oxalate of lime occurring in urine within twelve hours after emission is due to that cause.

But it may be asked, if we thus limit, I may almost say discard, the uric acid hypothesis, How are we to account for the frequent appearance of oxalate of lime in the urine? The reply is to be found in the fact that oxalic acid may be derived from a variety of sources, and is found in the urine under a variety of clinical and pathological conditions.

1. *Directly from food by the ingestion of substances containing oxalate of lime.*—It is a well-known fact that oxalate of lime crystals have been found in abundance in the urine of persons who have attempted to poison themselves with oxalic acid; and experiments* have shown that when non-poisonous doses are taken about twelve per cent. of the acid taken by the mouth appears

* Bucheim and Piotrowsky, quoted by Beale: 'Kidney Diseases and Calculous Disorders,' p. 381. Third edition. See also experiments by Dr Dyce Duckworth and Dr Leared, 'St. Bartholomew's Hospital Reports,' 1866, and 'Med. Times and Gaz.,' 1867.

as a lime salt in the urine. Many fruits and vegetables, such as rhubarb, sorrel, tomatoes, onions, and turnips, contain crystals of oxalate of lime; and to many persons in weak health, indulgence in such articles is invariably followed by an attack of indigestion and the appearance of crystals of oxalate of lime in the urine. It has, however, been urged that oxalate of lime cannot thus be absorbed from the intestine into the system and pass out unchanged into the urine, on account of its great insolubility in water. Reoch, however, has demonstrated that the insolubility is exaggerated, and he points out that Storer, in his 'Dictionary of Solubilities,' gives the solubility of oxalate of lime in water as $\frac{1}{300000}$. This, no doubt, appears small; but as oxalates are never recognisable without the microscope and seldom appear larger than a blood-corpuscle, so that, as Reoch argues, by taking the specific gravity of an average crystal as equal to a cube of water $\frac{1}{3000}$th of an inch in the side, since cubes are to one another as the cubes of their sides, it follows that a cubic inch of water would be equal to 27,000,000,000 of these crystals, and would therefore, according to Storer, dissolve 54,000, and ten ounces of water would dissolve 1,000,000 of these crystals; hence, as we do not often meet with a larger proportion than this in the urine, the amount of blood circulating in the body is more, considerably more, than sufficient to keep this quantity in solution. Urines containing oxalate of lime directly derived from the food are rarely altered in their general characters, and the crystals cease to be deposited at no very distant period after their ingestion. No sense of discomfort may be occasioned by their passage through the system, at most a mere passing attack of indigestion or increased urgency during micturition if there be any urethral or vesical disease, caused

by the passage of the crystals over the already sensitive mucous membrane.

2. *Indirectly from food, incomplete oxidation of the saccharine, amylaceous, and oleaginous principles of the food.*—Before their final conversion into carbonic acid and water these principles yield several intermediary non-nitrogenous acids, of which the chief are glycolic, lactic, and oxalic acids. The albuminous principles, besides yielding certain nitrogenous bodies, as leucin, kreatin, uric acid, and urea, also furnish a series of non-nitrogenous fatty acids similar to those obtained from the saccharine and amylaceous principle. Now, in the downward progress of these acids towards their lowest term, carbonic acid and water, it is quite possible that arrest of oxidation may take place at any one of them; and that whilst perfectly normal action produces carbonic acid and water, a check to the process will lead to the appearance of oxalic acid in the urine. Indeed, it is probable that there are many conditions within physiological limits in which power is economised in the system by eliminating the lower oxidised product, oxalic acid, by the urine instead of in its completely oxidised state, as carbonic acid, by the lungs. Oxalic acid formed under these circumstances will only occasionally be present in the urine, and will often appear and disappear without any apparent alteration in health. When the crystals of oxalate of lime are deposited in these cases they will be found in the urine passed within a few hours after food, their presence often inducing profuse urination.

3. *From increased tissue metabolism.*—As stated above, the albuminous principles by oxidation break up into two parallel series; nitrogenous bodies and non-nitrogenous fatty acids. When, therefore, increased metabolism of tissue occurs within the body, we have an

increase of these products in the urine. This is probably the most frequent cause of the appearance of oxalate of lime deposits in the urine, and they are met with under a variety of pathological conditions, frequently during the course of most febrile diseases, in pulmonary and cardiac affections in which respiration is impeded, and in disorders of the hepatic functions and depressed conditions of the nervous system. The urines in these cases are generally of a deep orange colour, of high average specific gravity, with an excess of urea and phosphoric acid, and are usually turbid with mucus and urates, while the deposits of oxalates are not usually persistent, often disappearing for a few days, to return again in great abundance. The oxalic acid in this case probably is, from reasons already stated, not derived from the decomposition of uric acid, either in the blood or subsequently in the urine after emission. The most rational explanation of its appearance being, that the process of oxidation within the body, under circumstances of increased tissue metabolism, is only sufficient to reduce a certain quantity of non-nitrogenous fatty acids formed within the body to their lowest term of carbonic acid, and consequently oxalic acid, which is one of the series, appears in the urine.

4. *From the mucus of the urinary passages.*—Crystals of oxalate of lime have been found in the mucus of the gall-bladder and in the gravid uterus, and it has therefore been suggested that the crystals that appear in the urine may have their origin in the mucus of the genito-urinary passages. In some cases this is probably true, but in the majority of instances we have no evidence of any morbid condition of the urinary passages to account for their appearance. It is probable, however, that calculi composed of oxalate of lime result

from chemical changes taking place in the mucus of the urinary passages, for, as Professor Parkes has remarked, "no one can observe the enormous amount of oxalic acid in calculi and believe that such abundance could ever come from the blood."* A very ingenious hypothesis has been advanced by Meckel† to account for this formation of oxalate of lime in mucus, by assuming that the mucous membrane of the urinary passages becomes the seat of a specific catarrh. In this catarrh a tough adhesive mucus is secreted, which has a tendency to undergo acid fermentation, and in which oxalate of lime appears when such fermentation occurs. At first this oxalate of lime mucus is of gelatinous consistence, but gradually it takes up more and more oxalate of lime from the decomposed urine, and thus, growing more and more firm, a stony concretion is at length formed. The large and numerous crystals of oxalate of lime so frequently observed in the urine of persons suffering from spermatorrhœa are most probably derived from the mucus of the genito-urinary passages; for if a patient suffering from this malady be directed to collect the urine passed at stool in a small vessel, and also the seminal and mucous discharge which generally follows micturition during the act of defæcation separately in a test-tube or on glass-slide, it will be found that both the urine and the discharge contain oxalates, which are, moreover, intimately mixed up in the latter, thus indicating an intrinsic origin. It is not improbable that the oxalate of lime deposits so frequently observed in the urines of ataxic patients, especially during the so-called *urinary crises*, may originate in this way, owing

* Op. cit., p. 223.

† 'Text-book of Practical Medicine,' by Dr F. von Niemeyer, vol. ii, p. 74.

to an abnormal condition of the mucous membrane of the urinary passages resulting from disturbed innervation.

5. *From excess of acid in the system.*—Beneke has pointed out that the increased production of lactic and butyric acids in the alimentary canal is frequently associated with oxaluria, since, as he thinks, the excessive formation of these acids prevents the development of the red corpuscles, so that oxidation is insufficiently performed. A catarrhal condition of the mucous membrane of the intestines he also pointed out as being frequently found accompanying this condition; he does not, however, consider it as being a proximate, but only a determining, cause of the disorder. Whilst endorsing Beneke's statement that deposits of oxalate of lime are met with in persons suffering from dyspepsia, attended with excessive formation of lactic and butyric acids, I do not consider his explanation to be the correct one, since in these cases I believe a catarrhal condition of the mucous membrane of the digestive canal to be the proximate cause, which, by hindering the onward passage of the food, favours fermentative changes and the production of lactic and butyric acids. These acids, which are formed in small quantities in the large intestine in health, being absorbed into the blood, are normally reduced to carbonic acid, which under ordinary circumstances passes off with the other carbonic acid formed in the body by the lungs. If, however, the process of respiration be at all impeded, some of the carbonic acid may be eliminated by the urine, combined with the oxides of potash and soda, in the form of alkaline carbonates, causing an alkaline condition of that secretion (pp. 47—53).* Or if the acids absorbed from the intes-

* 'The Lancet,' July, 1880. "A Form of Dyspepsia associated with an Alkaline Condition of the Urine." By the Author.

tinal canal into the circulation be formed in excess, their reduction into carbonic acid may be incompletely performed, and so the intermediate acid, oxalic, appears in the urine in combination with lime. It is this condition, and this condition only, to which I think the term "oxaluria" may be clinically applied with a fair show of reason, since the chief and most persistent urinary phenomenon is the deposit of oxalate of lime crystals in the urine.

The symptoms which attend this form of dyspepsia are in typical cases sufficiently characteristic to distinguish them from those which accompany the derangements associated with deposits of uric acid, and which the late Dr Murchison so graphically portrayed in his account of the condition he termed "lithæmia."* Thus the sufferers from oxaluria are to be found chiefly among the careworn, the harassed, the overworked, and underpaid members of the community, and form a marked contrast in appearance to the generality of those troubled with uric acid tendencies; whilst high living combined with sedentary habits tends to promote a condition of "lithæmia," so that persons suffering from that form of dyspepsia, instead of feeling refreshed by food, are seized "with a feeling of oppression, often of weariness and aching pains in the limbs, and an insurmountable sleepiness after meals" (Murchison). On the other hand, patients with oxaluria feel for a time better after food and improve on a generous, if suitably selected, dietary. Again, a tendency to uric acid deposits is more frequently met with among dwellers in towns, whilst, as far as my experience goes, the victims of oxaluria are most frequently country patients, especially those residing in damp and marshy districts, or on cold ill-drained clay

* 'Lectures on Diseases of the Liver,' 2nd edition, p. 566.

soils; situations, in fact, in which catarrhal affections of the intestinal canal are likely to be engendered. Although in both conditions the mental state is more or less affected, still it assumes a different aspect in each. In "lithæmia" the patient is irritable, fretful, peevish, and discontented with those around him, but he is rarely at fault with himself or hypochondriacal. In oxaluria, however, the patient is generally amiable and easy tempered with his relations and dependents, but is himself filled with the deepest gloom and forebodings, and is painfully hypochondriacal. In oxaluria the bowels are irregular, constipation at times alternating with a colicky diarrhœa of frothy, yeasty character, and not infrequently accompanied with considerable discharges of blood. The urine is usually of a pale greenish colour, and the quantity passed in the twenty-four hours normal in quantity and specific gravity. Its chief characteristic is the deposit of crystals of oxalate of lime, which are found most abundantly in the morning urine passed on first rising. Owing to the presence of these crystals causing irritation of the mucous membrane of the bladder, micturition is frequent and urgent, though the quantity of urine passed is not large. Traces of sugar are not infrequently present, and sometimes sugar for a while replaces the deposit of oxalates, and *vice versâ*. This transformation has been accounted for by the hypothesis that whilst oxalic acid denoted a condition of imperfect oxidation, sugar represented a still lower. The appearance therefore of oxalates with a diminution of the excretion of sugar has frequently been taken as a favorable symptom of diabetes, an opinion, however, which I do not think altogether warranted. The urine occasionally contains an excess of phosphate of lime, though this condition is not nearly so frequently observed in this

form of oxaluria as in the case where the deposit of oxalate of lime results apparently from increased tissue metabolism, and in which, as has been already stated, an increase of urea is also generally noted. Various reasons have been assigned to account for the associations of deposits of oxalates with occasional excess in the elimination of phosphate of lime in the urine. The most probable explanation is that it originates in two ways: —*a*. In those cases where there is an excess of urea the increase in the elimination of the phosphoric acid is the result of the increased metabolism of the tissues generally. *b*. Where the deposits of oxalate of lime are associated with catarrh of the intestinal canal, and the formation of lactic and butyric acids is excessive, the phosphate of lime is derived not from the tissues, but from the alimentary canal, the lactic acid having a powerful solvent action on this salt; so that if it is introduced in excess with the food, a larger proportion will be dissolved out and pass into the system than would otherwise be the case. In addition to the mental depression already mentioned, patients suffering from this form of oxaluria are troubled with many anomalous symptoms indicative of nervous disturbance. Thus, a burning sensation is usually felt across the loins, accompanied by a feeling of tightness and dragging round the abdomen, shooting and burning pains in the lower limbs, twitching of certain groups of muscles, with often a feeling of numbness, deadness, and coldness in different parts of the body. These symptoms, when present together, may lead us to infer that the patient is suffering from an early stage of locomotor ataxy, as was the case with an out-patient at present under my care at the London Hospital, when he first came under observation. The fact, however, that other characteristic symptoms

were absent, and did not develop, and that he improved on a treatment directed to the relief of the dyspeptic condition, dispelled any doubts on that point.

With regard to the treatment of the conditions we have been describing. In those cases where the deposit manifestly arises from the ingestion of articles of food containing crystals of oxalate of lime, it will be sufficient to point out what these are and to discontinue their use. If the deposits arise indirectly from the food, owing to incomplete oxidation of the saccharine, oleaginous, and albuminous principles, it will be necessary carefully to regulate the diet with regard to quantity and quality, and to promote the oxidising processes within the body by means of iron, change of air, sea-bathing, &c. In those cases where oxalate of lime deposits seem to arise from increased tissue metabolism, as evidenced by an increase in the amount of the urinary constituents, more especially the urea and phosphoric acid excreted daily, inquiry must be made into the nature of the conditions producing such disturbance, and the treatment directed accordingly. In the case of calculous deposits of oxalate of lime it will be profitable to remember that the oxalic acid has possibly its origin in the mucus of the urinary passages, and not necessarily in the blood, a reflection which ought to direct our attention rather to the treatment of any local morbid condition that may exist in them than to the employment of remedies designed to act on the system generally. Lastly, with regard to these cases of dyspepsia associated with more or less persistent deposits of oxalate of lime, and to which alone, as I have stated, the term "oxaluria" seems applicable. Our effort at treatment must be directed, almost entirely to the relief of the catarrhal conditions on which the dyspeptic symptoms depend. This is best

effected by the systematic employment of small doses of Carlsbad salts largely diluted; a teaspoonful of the salt dissolved in ten to fifteen ounces of hot water, as hot as the patient can bear it, should be taken every other morning an hour before breakfast. This diluted warm saline solution seems to have the power of dissolving and removing a considerable quantity of the abnormal mucus, which in undergoing fermentative changes gives rise to lactic and butyric acids, the motions which result from its use containing not only fæcal matter, but much offensive glutinous-looking slime. Thirty-grain doses of bismuth should be administered once or twice a day before meals, and Dr Prout's mixture of nitro-muriatic acid and nux vomica may be prescribed with advantage, especially in long-standing cases when there is much mental depression, about two or three hours after food. The patient should remove to a dry soil, but if that is not possible the greatest attention should be paid to the subsoil drainage of his house. The use of a cold-water compress over the abdomen at night will be found advantageous, not only in relieving the abdominal catarrh, but in protecting the patient against a return of the malady. The diet should be nutritious and digestible, with a liberal allowance of meat, fish, poultry, and game. The bread should be eaten stale, or, better still, toasted. Sugar and all farinaceous food should be avoided as much as possible without actually restricting them, and flatulent vegetable food altogether discarded. Tea may be used in moderation, but coffee and alcohol are positively injurious.

CHAPTER VI

DERANGEMENTS ASSOCIATED WITH THE EXCESSIVE ELIMINATION OF PHOSPHORIC ACID

The amount of phosphoric acid passing out of the system in the course of the twenty-four hours averages from 2·5 grammes to ·3 grammes, and is distributed among the four bases, potash, soda, lime, and magnesia, in the proportion of about two thirds combined with the alkaline oxides and one third with the oxides of the earths. The alkaline phosphates are extremely soluble, and therefore are never deposited from the urine. On the other hand, the earthy phosphates are only soluble in acid solutions, so that when the urine becomes neutral or alkaline they are deposited. Thus it happens that a deposit of the earthy phosphates is by no means an indication that they are in excess any more than the fact that no deposit is present is an assurance that they are being excreted in normal amount. So long as the urine remains acid a considerable quantity of phosphoric acid may be passing out of the system without giving evidence of its presence, whilst if the urine from any cause becomes alkaline a deposit at once occurs, although the phosphoric acid may not be eliminated in excess. It is, therefore, of the greatest importance to determine quantitatively the amount of phosphoric acid passing out of the system daily in any doubtful case;

since the deposits dependent upon an alkaline condition of the urine have rarely a grave import, except those connected with the triple phosphate, whilst persistent excessive elimination, with or without deposition of the earthy phosphates, is generally associated with grave constitutional disturbance.

When human urine becomes alkaline it is due to one or other of the following conditions:—1. To excess of the *fixed* alkalies, chiefly the alkaline carbonates of potash, and to some extent of alkaline phosphates of the same bases. 2. To the presence of volatile alkali by the formation of ammonia in the urine from decomposition of the urea.

The conditions which lead to the excessive elimination of the carbonates of potash and soda, by which the alkaline condition of the urine due to fixed alkali is almost entirely produced, have been already discussed at length (pp. 47—53), and therefore need not be entered upon again. It is, however, necessary to point out that the urine in these cases is not always distinctly alkaline, but often neutral and even faintly acid, and that no deposition of earthy phosphates is observed till the urine is boiled, when a white cloud of phosphates is precipitated. On testing the urine now with litmus paper it will be found to be distinctly alkaline, the heat having expelled the carbonic acid held in solution, and which gave to the urine its faintly acid reaction. If a few drops of mineral acid be added to the urine with a view of discovering whether the precipitate was caused by albumen or by phosphate of lime, brisk effervescence occurs, showing that carbonates are present in considerable amount.

When the urine is alkaline from the presence of *volatile* alkali we have, in addition to the deposit of phos-

phate of lime, crystals of ammonium magnesium phosphate. The ammoniacal condition of the urine is due to a ferment which can be isolated by filtration; it consists of spherical globules which settle at the bottom of the vessel and appear to increase by budding. This ammoniacal fermentation of the urea takes place in the urine only after its secretion by the kidneys, and does not occur in normal urine unless it becomes mixed with the products of decomposition from the mucus of genito-urinary tract, or the ferment introduced into the bladder by dirty catheters, or the urine already alkaline from fixed alkali is received into dirty chamber vessels. I have already (p. 49) explained how the irridescent film, consisting of crystals of ammonium magnesium phosphate, occasionally found on the surface of urine of persons suffering from flatulent dyspepsia is due to the latter cause. The presence, therefore, of crystals of triple phosphate when persistent in the urine are indicative of local disease of the urinary organs, and not the direct result of constitutional disturbance. The treatment of ammoniacal urine must therefore be directed to the relief of the morbid conditions existing in the genito-urinary tract and the destruction of the ferment. It is a condition that is often extremely difficult to deal with, but the plan of treatment I have found the most satisfactory is the persistent administration of benzoate of soda combined with turpentine and opium,* and washing out the bladder twice a week with a one per cent. solution of hydrochloric acid.

When, however, we have to deal with the persistent elimination of phosphoric acid in excessive quantities

* ℞ Sodæ Benzoat., ʒss; Olei Terebinthinæ, ʒj; Liq. Opii Sed., ʒss; Syrupi Tolutanæ, ʒss; Mucilaginis Acaciæ, ℥j; Aquæ ad ʒvj. Two tablespoonfuls three times a day.

very distressing constitutional symptoms are associated with its discharge. The symptoms vary considerably in individual cases, but they are all more or less characterised by great nervous irritability, derangements of digestion, great emaciation, severe aching pains in the back and loins, especially affecting the pelvic viscera. The urine is copious, of medium specific gravity, either acid and clear, but more frequently alkaline, and whey coloured from the deposited phosphates. As the disease advances symptoms analogous to those of diabetes, especially of the insipid form, make their apearance; indeed, the disease seems to merge into that condition insomuch that it has been proposed to give to this disorder the distinctive title of "phosphatic diabetes."

Under the terms Diuresis, Diabetes insipidus, Polyuria, and Polydipsia, writers have described a certain morbid condition of the system characterised by the excessive and persistent discharge of urine of low specific gravity—containing, however, neither sugar nor albumen. Most authors apply either of the above terms to denote this urinary superflux, without reference to the quantitative relationship that may exist in individual cases between the urinary water and solids. Others, of whom Willis* seems to have been the first, have attempted to form a classification on this basis. Thus Willis divided cases of diabetes insipidus into three groups:—(1) those attended with excessive discharge of aqueous urine, in which the solid matters are deficient—*hydruria;* (2) those attended with a copious discharge of urine characterised by a deficiency of urea—*anazoturia;* and (3) those in which the excessive discharge of urine was

* Robert Willis, M.D., 'Urinary Diseases and their Treatment.' London, 1838.

attended with a superabundance of urea—*azoturia*. Parkes* also supported the view that diabetes insipidus was to be found existing under three different conditions—(1) In cases where there is no increase or decrease of tissue metamorphosis; (2) in cases where there is a decided decrease of tissue metamorphosis; (3) cases where there is evidence of increased tissue metamorphosis, as shown by the increase of some of the urinary solids. To this latter class of cases Professor Parkes thinks the term polyuria preferable to that of azoturia, which only expresses the fact of the urea being increased; whereas in the cases quoted by him the fixed salts, as chlorides, sulphates, and phosphates, were also present in abnormal quantities. Lastly, the term "baruria," which was first introduced by the late Dr Fuller in describing certain forms of dyspepsia associated with excess of urea in the urine, might be advantageously employed when only the solid matter is increased but not the water. Lately, Dr Tessier† of Lyons has recorded a series of cases closely resembling saccharine diabetes, in the increased discharge of urine, the thirst, the neuralgic and rheumatic pains, the wasting, and the secondary lung complications, only that no trace of sugar could be found in the urine, and that the constant phenomenon was a very considerable increase in the quantity of phosphoric acid excreted (fifteen to twenty grammes of earthy phosphates in twenty-four hours). In some of Dr Tessier's cases the urea was also eliminated in excess, but not in all, a fact which Dr Tessier thinks serves to distinguish them from

* Ed. Parkes, M.D., F.R.S., 'The Composition of the Urine in Health and Disease.'

† L. J. Tessier, 'Du Diabète Phosphatique.' Paris, Ballière et Fils, 1877.

the cases originally described as "azoturia." Dr Tessier has given the name "phosphatic diabetes" to this class of cases. He divides them into four groups—1. Those in which nervous symptoms are predominant. 2. Those which accompany pulmonary consumption. 3. Those which alternate with or coexist with saccharine diabetes. 4. Those which run a distinct course resembling saccharine diabetes, but without sugar. As a few cases resembling in many respects those described by Dr Tessier have come under my observation, although in none of them were the symptoms so marked or the excretion of phosphoric acid so considerable as in those described by him, I give a brief account of them, since they may be of some service in illustrating this interesting and obscure point in urinary pathology.

Case 1. *Polyuria with increased excretion of phosphoric acid and urea; nervous symptoms.*—J. H.—, aged sixteen, was admitted into the Seamen's Hospital July, 1876, in a stupid, semi-comatose condition, extremely feeble, and emaciated. Weight under 9 st.; no great thirst; passing large quantities of urine of medium specific gravity with trace of albumen; no sugar. No history of syphilis or injury to the head. Analysis of the twenty-four hours' urine gave the following result:

Quantity	... ...	2900 c.c.	
Specific gravity	... ...	1010	
Earths, Alkalies	(phosphoric acid)	2·3, 2·9	5·2 grammes.
Urea	... ...	51·	grammes.

The lad remained in bed for several days in a dull, stupid condition, and then gradually brightened. The diuresis continued excessive during the whole period of

his stay in hospital, the specific gravity ranging from 1010 to 1015. He was treated successively with large doses of valerian, with small doses of opium, with cod-liver oil and quinine. He improved greatly under treatment with regard to his general condition, but he was still polyuric when discharged. In this case the quantity of urine passed was about three times, the solids about double (calculated from the specific gravity), the phosphoric acid more than treble, and the urea rather more than double the normal for a lad of his age. In this case there was a decided increase of tissue metamorphosis, as evidenced by excessive excretion of urea and phosphoric acid, the latter especially. It comes under Dr Parkes' third definition, and corresponds with the first group of Dr Tessier.

Case 2. *Polyuria; increased elimination of phosphoric acid; death; small syphilitic gumma at base of brain.*—T. G—, aged twenty-four, a patient of the late Dr Murchison, came under my observation on August 24th, 1878, during Dr Murchison's absence from town. The patient, a slight man weighing about 9 st., had been ailing four or five months; sight failing for a month, but has got rapidly worse during the last week; cannot now read or count fingers when held up. Passing large quantities of water; syphilis five years ago. Ophthalmoscopic examination only revealed slight fulness of veins. He was instructed to collect and measure urine and bring some for analysis next visit. August 28th.—Patient much worse; complains of violent pain in head. Quantity of urine passed in the last twenty-four hours 9500 c.c.; reaction neutral; sp. gr. 1004; phosphoric acid 6 grammes. August 30th.—Violent pain in head; now quite blind; as he required more care and attention

than he could in his circumstances receive at home he was taken to St. Thomas's Hospital. Here, shortly after admission, he became delirious, and then comatose, and died on September 2nd. I am indebted to the courtesy of the then house-physician for a note with regard to the condition of the brain as found at the post-mortem examination:—"A small syphilitic gumma, about half the size of a small hazel-nut, situate in the middle line under the floor of the third ventricle, obstructing some of the vessels at the base; some softening of the brain substance."*

CASE 3.—*Polyuria moderate; increased elimination of phosphoric acid; hypochondriasis; rheumatic pains in loins; emaciation.*—Out-patient, under my care at the London Hospital. First seen September 16th, 1880. A small but well-built man, aged twenty-five, weighing about 9 st., employed on the East London Railway; attributes his illness to over-work. No history of syphilis. Temperate habits. Has a pale, anxious, haggard expression. States that he has been ailing some months, has lost flesh, and complains of a feeling of extreme nervousness and exhaustion, with frequent fits of trembling. Constant tearing pains in loins, often shooting round the pelvic region, with cramp-like spasms in lower parts of abdomen. No lightning pains, patellar reflex unimpaired. Vision perfectly distinct.

* This case was plainly one of hydruria, or diabetes insipidus, without increased tissue metaphorphosis, the diuresis being a consequence of the cerebral lesion. The increase of the phosphoric acid (nearly treble the normal) is, I think, sufficiently accounted for by the large quantities of milk and beef-tea taken to quench thirst at that period of the illness when the analysis was made, and also to some extent to the washing out of the tissues by the drainage going on through the body.

No apparent disease of abdominal or thoracic viscera. Digestion fairly good; bowels constipated. Urine pale, whey-like, of medium specific gravity; alkaline reaction; no sugar; no albumen. States that he passes more urine than he should, and is frequently disturbed at night to pass it. Instructed how to collect and measure it, and to bring a sample of the mixed twenty-four hours' urine at the next visit. The patient, however, did not comply with all the conditions necessary for accurate measurement, and it was not till Oct. 21st that I was satisfied that my instructions had been carefully carried out. By that time he had been five weeks under treatment (mineral acids and nux vomica), and had improved to some extent. Analysis of twenty-four hours' urine: Oct. 21st.—Quantity 2300 c.c.; sp. gr. 1015; reaction alkaline. Phosphoric acid 7·8 grms., treble what it should be for a man of his weight. Ordered codeia pill, one third of grain, and a mixture with bromide of potassium and nux vomica. Nov. 18th.—Very much improved; is gaining weight, feels stronger, has nearly lost the pains, discharge of urine still more abundant than it should be. To collect and measure it as before and bring a sample at next visit. To continue mixtures but to discontinue the codeia. Nov. 25th.—Analysis of urine: quantity 2300; sp. gr. 1015; reaction alkaline. Phosphoric acid 5·8 grms.; urea 33·5 grms.

Continued to attend off and on as an out-patient till November, 1881. His general condition was then much improved, and he resumed regular work.

Case 4. *Excessive elimination of phosphoric acid; no polyuria; hypochondriasis; enormous quantities of calcium oxalate in urine.*—A gentleman's servant, aged twenty-seven. First came under observation Sept. 28th, 1880.

He is a thin spare man, weighing about eight and a half stone; of sallow, haggard complexion. No history of syphilis; habits temperate. Complains of aching pains, especially in the loins, shooting down the hips, and occasionally affecting the bladder and testicles. Alleged loss of virile power. Abdominal and thoracic organs apparently healthy. Digestion fair, bowels constipated. Feels very wretched and depressed. Urine passed at the time of visit (11 a.m.) acid; specific gravity 1028, containing 8 grms. of phosphoric acid in 1000 c.c. The secretion of urine, he said, was not excessive; he was rarely troubled during the day, but frequently at night, with calls to micturate. (He was requested to collect and measure the urine for a few days, and send a note with regard to the quantity passed in the twenty-four hours; this proved to be just under two pints, or about 1100 c.c.) The urine he passed in my presence deposited in a few hours an enormous quantity of oxalate of lime; no sugar; no albumen. Ordered codeia pill, a quarter of a grain, at night, and a mixture of hydrochloric acid in nux vomica and cod-liver oil. Nov. 18th.—Is much better. Less pain in loins. Not so despondent, though still fears he is impotent; confesses, however, to occasional manifestations of "his nature." To discontinue codeia and take phosphorus pills, one sixtieth of a grain, instead. To collect urine for twenty-four hours and send it for examination. Dec. 1st.—Quantity 1520 c.c.; sp. gr. 1022; urea 41·2 grms.; phosphoric acid 5·2 grms.*

Case 5. *Polyuria; increased elimination of phosphoric acid, co-existing with a mild form of glycosuria.*—A

* This case corresponds with those originally described by Beneke of phosphaturia combined with oxaluria. 'Zur Phys. und Path. des Phosphors und Oxalsaure,' Kalkes, 1850.

gentleman, aged thirty-seven, who for the last eighteen months has suffered intermittently from a mild form of glycosuria, which did not apparently affect his general health, began in the autumn of the present year (1880) to suffer from constant aching, boring pains in the loins, shooting round the pelvic regions, with occasional cramp-like sensations in the bladder, and a tired, sore feeling in the muscles of the thighs and calves of the legs. He also became dispirited and hypochondriacal; began to lose weight and flesh. The amount of sugar passed had never been excessive, and had always been controlled by restricted diet. At this time he was certainly not passing more sugar than he had done in the earlier stage of his illness, and it again disappeared when he placed himself on restricted diet for a few days. Still, however, the pains and malaise continued.

On Oct. 12th the urine was collected for twenty-four hours, and subsequently on Oct. 14th and 15th, and Nov. 3rd, 21st, and 26th. On each occasion the amount of phosphoric acid present was estimated with the following results:

	Quantity.	Sp. gr.	Phosphoric acid.	Sugar.	Urea.
Oct.	12th 2020 c.c. ...	1018 ...	7·6 grms. ...	nil.	—
„	14th 2300 c.c. ...	1015 ...	6·9 „ ...	nil.	—
„	15th 1520 c.c. ...	1020 ...	5·7 „ ...	nil.	—
Nov.	3rd 2500 c.c. ...	1012 ...	7·5 „ ...	considerable	—
„	21st 2350 c.c. ...	1019 ...	8·2 „ ...	„	—
„	26th 2300 c.c. ...	1018 ...	4·6† „ ...	„	69 grms.

The patient began taking codeia in half-grain doses at bedtime on the night of Oct. 12th, and continued to take it till Oct. 25th; it was then discontinued, as he was feeling better. On Nov. 3rd the pains, however,

† Phosphoric acid in combination with the earths, 2·1 grms.; with the alkalics, 2·5 grms.

returned with considerable severity, and the codeia was resumed, but it was only taken occasionally up to Nov. 20th. Sugar also reappeared in the urine in more considerable amount than had been previously noted, and continued till the patient left town. No special reason could be assigned for the reappearance of the sugar, as the diet was in no way different on the days of its reappearance than it had been during the period immediately preceding. That is to say, the diet had been restricted, with the exception of a small quantity of crust of bread taken with each meal. Grain doses of extract of opium were now given at bedtime till Dec. 4th, when the patient left town for a month's rest. During that time he took no medicine. Most of the holiday was spent at watering-places, where he bathed daily and made use of tepid saline douches; he also took a considerable amount of walking exercise. He returned to town feeling better in every respect. He has regained his lost weight, and is now bright, cheerful, and hopeful. The pains in the loins and thighs still, however, trouble him occasionally. The urine (Jan. 15th) on examination gave the following result. Quantity 1900 c.c.; sp. gr. 1020; urea 66 grms.; phosphoric acid 3·8 grms.; no sugar.

Since the last note up to Feb. 14th, 1882, the patient's health, with the exception of temporary attacks of glycosuria, has continued to improve.

Case 6. *Polyuria; excessive elimination of phosphoric acid and urea.*—J. G—, aged twenty, was admitted into the Seamen's Hospital on Nov. 13th, 1877, suffering from extreme debility and prostration, and complaining of pain in all his limbs, and especially across the loins. His face was somewhat flushed and the eyes bright, but

the temperature was normal; the pulse weak and feeble; chest sounds natural, with the exception of some coarse râles in the large bronchial tubes. Urine clear, acid; no albumen; no sugar. He says the present illness commenced three weeks previous to admission, but he had otherwise always enjoyed good health. During this attack he had lost eighteen pounds in weight. He has a spinal curvature, the seventh and eighth dorsal vertebræ being the bones affected, and he has also a strumous appearance generally. On Nov. 19th, seven days after admission, the mucous râles in the chest had cleared up, and he was not so prostrate. The pulse was stronger, and the temperature had remained normal during the time he had been in the hospital. Still the patient, in the absence of any definite symptoms, was extremely feeble and weak. Although no sugar had been found in the urine, it was thought advisable to collect the urine for twenty-four hours, and then test for that substance in the whole quantity. Nov. 20th.—The urine collected during the last twenty-four hours measured 4600 c.c., and had a specific gravity of 1010, but gave no reaction with Fehling's solution. Nov. 21st.—The quantity of urine collected in twenty-four hours measured 1400 c.c., a nearly normal quantity, but the specific gravity had risen to 1029, so that the relationship between the solids excreted on each day was tolerably constant, and exceeded by a third the normal excretion. The urine was collected, measured, and the specific gravity taken subsequently each day during the patient's stay in the hospital; but it will be sufficient here to state that the average quantity passed by the patient each day for a month was 3263 c.c., with a specific gravity of 1017. Taking the healthy excretion of an adult so be at the outside 1500 c.c., with a specific gravity of 1020,

the patient was passing more than twice the normal quantity of urine, and excreting one third more than the ordinary quantity of urinary solids.

The urea and phosphoric acid were determined quantitatively on several occasions by the house-physician, Dr Murphy, with the following result:

Date.	Quantity of Urine. C.c.	Sp. gr.	Urea. Grms.	Phosp. Acid. Grms.
Dec. 3rd	4476	1011	67	5·3
„ 4th	4800	1016	116	9·6
„ 5th	4100	1018	103	9·0
„ 7th	3050	1017	61	4·28

On the 13th of December I made a quantitative estimation of the urea and the earthy and alkaline phosphates, with standard solutions distinct from those used by Dr Murphy, and my results closely corresponded with his—viz. quantity 2700 c.c., total urinary solids 108 grms., urea 89 grms. Phosphoric acid in combination with lime and magnesia 1·8 grms.; phosphoric acid in combination with the alkaline oxides 3·7 grms.; total phosphoric acid 5·5 grms. Diet: 4 oz. wine, milk 2 pints, strong beef-tea 1 pint, bread 12 oz. The patient remained in hospital till the 20th December, when he was removed by his friends. His condition was materially improved, and he had regained 15 lbs. of his lost weight, but the urinary secretion was not diminished. During his stay in hospital the patient suffered greatly from boils. The patient had no dimness of sight, nor any appearance of cataract. At no time could even minute traces of sugar be discovered in the urine. This may be considered as a typical case of diabetes insipidus, accompanied with increased metamorphosis of tissue. It resembles Willis and Prout's cases of azoturia, and also corresponds to Tessier's fourth group.

The particulars of the six foregoing cases may thus be briefly summarised:

	Age.	Approximate weight.	Quantity.	Sp. gr.	Phosp. Acid.	Urea.
Case 1	...16...	8 st. 7 lb.	....2900 c.c.	...1010	...5·2 grms.	....51·0 grms.
„ 2	...24...	9 st.	...9500 „	...1004	...6·0 „	—
„ 3	...25...	9 st.	...2300 „	...1015	...7·8 „	...33·5 grms.
„ 4	...27...	8 st. 7 lb.	....1520 „	...1022	...5·2 „	...41·2 „
„ 5	...37...	12 st. 7 lb.	....2020 „	...1018	...7·6 „	—
„ 6*	...20...	9 st.	...3825 „	...1016	...6·7 „	...87·2 grms.

In all the increase of phosphoric acid over the normal excretion was considerable. If we except Case 2, they differ from the ordinary hydruric forms of diabetes insipidus, in that the discharge of urine, though considerably more than normal, in no way approached the enormous superflux met with in that form of the disease.† On the other hand, the cases in many respects resemble those related by Prout and Willis, and to which those authors gave the title azoturia. As, however, these observers did not estimate the phosphoric acid excreted as well as the urea, it is impossible to say in their cases whether it was increased or not. Dr Parkes,‡ however, quotes a case of Vogel's, which seems closely to correspond with the instances I have given, and in which the following amounts were passed in two periods of twenty-four hours respectively: Quantity 2800 c.c. and 3600 c.c.; urea 40·6 grms. and 47 grms.; phosphoric acid 4·1 grms. and 8·3 grms. In this case the urea as well as the

* Average of five observations.

† It may be as well to mention that, though reference is only made to the quantity of urine and the specific gravity on those days when an estimation of phosphoric acid was made, yet observations on this point were frequently made in each individual case, and the relationship was found to be pretty constant.

‡ Op. cit., pp. 10, 367.

phosphoric acid was increased, though the proportionate increase of the latter over the former in the second analysis is prodigious. This is what Dr Tessier contends for when he gives the distinctive title "phosphatic diabetes" to this form of diuresis accompanied with increased elimination of phosphoric acid; for though urea in some of his cases was in excess, it was not so in all; and this, he says, is the point that distinguishes between azoturia and phosphaturia. Of my cases, in Case 1 and Case 4 the urea was about one third in excess, whilst the phosphoric acid was more than double the normal excretion. In Case 6 the urea was more than double, and the phosphoric acid treble, the normal. In Case 3 the amount of urea was normal, whilst more than double the usual amount of phosphoric acid was excreted.* In these cases, therefore, the excess in the elimination of phosphoric acid was proportionately larger than that of the urea.

The question may now be asked, Whether increase of phosphoric acid is not a constant phenomenon in all cases of diuresis, or whether it may not be accounted for by the increased ingestion of food and by the washing out of the tissues by the drain of water through them? Analytical evidence on this point is meagre, but what evidence we have shows that the increase in the quantity of food ingested, or the drain of water through the system, does not necessarily increase the elimination of phosphoric acid. Dickinson† and other observers‡ have

* Throughout I have assumed the 2·5 grammes represent the normal excretion of an adult weighing from 8 to 9 stone, and 3· grammes for an adult weighing 11 to 12 stone.

† W. Howship Dickinson, M.D., 'Diseases of the Kidney,' &c., Part 1, "Diabetes," pp. 173 and 208. London, 1875.

‡ Neubauer, Boecker, Beneke, Vogel, Gaethgens, quoted in Ziemssen's 'Cyclopædia,' Article "Diabetes."

remarked an increased elimination of phosphoric acid, especially in combination with the earths, in certain cases of diabetes mellitus, but this increase is very far from being universal, as other analyses prove (Parkes).* Again, in the cases of diabetes insipidus given by Dickinson, though an increase is noted in some, it is not in all; and in two cases, which I reported in the 'Lancet,'† the phosphoric acid was if anything decreased. For example, in one case in a man weighing 11⅓ st., the daily average secretion of urine was over 3000 c.c., whilst the phosphoric acid estimated on three occasions never exceeded 2·4 grms. In the second case the patient weighed 8½ st., the urine passed was 2400 c.c., and the phosphoric acid was only 1·6 grm. But if the exaggerated excretion of phosphoric acid is not a constant phenomenon of diabetes insipidus, to what are we to attribute its appearance in the exceptional cases? And here we pass from the consideration of facts to the region of conjecture. There is no question in scientific medicine on which we have fewer facts to generalise from than that concerning the elimination of "phosphates in disease," and consequently there are few subjects which have yielded a richer harvest to the quack. Physiology‡ can only tell us that the element phosphorus is absolutely essential for the growth and nutrition of the tissues, but cannot explain its *rôle*. Whilst, therefore, our information with regard to the physiological action of phosphorus within the body is still so scanty, it is obvious we are not yet in a position to indulge in speculations concerning the part played by it in the production of

* Op. cit., p. 344.

† 'The Lancet,' Feb. 26th, 1876.

‡ 'Text-Book of Physiology,' Michael Foster, M.D., F.R.S., p. 366. London, 1878.

certain pathological phenomena with which it has been associated. It is satisfactory, however, to know that the attention of scientific workers* has been called to this subject, and we may hope that shortly a sufficient number of trustworthy facts may be collected, which will enable us to gain a clearer insight into the part played by this important element with respect to the nutritive changes with which it is concerned within the body. Nor is clinical observation in this instance much in advance of our physiological and pathological knowledge. Excessive elimination of phosphoric acid has been noticed in acute inflammation of the membranes of the brain (Bence Jones), in the acute paroxysms of certain forms of mania (Sutherland and Beale), and after injuries to the head (George Harley). And the late Dr Golding Bird attributed some of the cases of phosphaturia that came under his observation to spinal lesions, probably functional in character. But whether in these conditions it is due to increased metamorphosis of the nervous matter or to the irritation of a still hypothetical "coördinating chemical centre," or to the influence of a disturbed condition of the nervous system upon nutrition generally, it is at present impossible to decide. Increased elimination of phosphoric acid, again, Beneke† has considered in some cases to be due to excessive formation of acid in the tissues, dissolving out the earthy phosphates; in these cases oxalates and

* W. Zulzer, 'Ueber das Verhältniss der Phosphorsäure zum Stickstoff in Urin," 'Centralblatt fur die Med. Wissenschaft,' 1876, p. 474. Von Prof. Dr. Edlessen in Kiel, "Ueber das Verhältniss der Phosphorsäure zum Stickstoff in Urin," 'Centralblatt f. d. Med. Wissenschaft,' 20 Julii, 1878. Emilie Lehmus, "Ueber der Relativen Wert der Phosphorsäure in Urin bei Kindern," 'Cbl. f. Kinderheilk.,' No. 19, 1878.

† Dr. F. W. Beneke, 'Archiv des Vereins,' p. 450. 1854.

phosphates of lime will both be found in excess in the urine. Similarly in certain cases of dyspepsia associated with excessive formation of lactic acid in the stomach and intestines, more phosphate of lime may be rendered soluble and absorbed into the system, and thus pass out by the urine instead of by the bowel. Marcet* has shown from analyses of pulmonary tissue in consumption that a considerable reduction of phosphoric acid and potash takes place, both in the insoluble tissue and nutritive material, as compared with healthy lung tissue. And Edlessen† has shown that the excretion of phosphoric acid is increased in cases of anæmia, especially pernicious anæmia. The observations of the authors I have quoted are, however, too limited to draw definite conclusions from as yet. All that we are warranted in assuming from them is, that increased excretion of phosphoric acid is met with in those states of the system which we characterise as "nervous," and that it is often met with accompanying or preceding diseases in which disorder of nutrition is usually well marked.‡

* W. Marcet, M.D., F.R.S., 'Experimental Inquiry into the Nutrition of Animal Tissues,' p. 47. London, 1874.

† Op. cit.

‡ It will be observed that I have not included rickets among the diseases in which an increased elimination of phosphoric acid is noticed. The truth is that the fact of there being an increase is by no means established. Professor Gamgee, in his recent work on 'Physiological Chemistry,' states that no reliable analysis has yet been made to prove it. Whilst Dr Seeman who has analysed the urine of sixteen rachitic children, has actually found a diminution, which was most marked when the disease was at its height. Dr Seeman regards the bone changes in rickets to be due to lime starvation, the salts of that base not being introduced in sufficient quantity into the system, owing to the catarrhal condition

With regard to the treatment of the form of disease under consideration, the main indications are rest and an endeavour to promote nutrition generally. To attain this end opium or codeia should be given in full doses, when the patient first comes under observation. As soon, however, as the nervous system is quieted, and the rheumatic and neuralgic pains are less severe, it should be discontinued, lest it interfere with digestion. General tonics, such as iron, phosphorus, quinine, nux vomica, hydrochloric acid, and cod-liver oil, should be persevered with. When there is a history of syphilis iodide of potassium should be combined with these remedies. Warm baths, followed by tepid douches, give great relief to the neuralgic pains, and also soothe the nervous system. The soluble phosphates may be administered; but their utility in these cases is questionable. There appears to be no lack of these constituents in the system; the difficulty seems rather to lie in the want of power of the tissues to retain them. The food should be light and nutritious, and milk one of the chief constituents. Alcohol should be avoided; it invariably, even in small quantities, increases the diuresis. The same may be said of coffee. Change to dry bracing air should be obtained if possible.* The clothing should

of the mucous membrane of the intestines hindering their absorption. ("Zur Pathogenese und Ätiologie der Rachitis," von Dr Seeman, 'Virchow's Archiv,' lxxvii, 1879.)

* By strictly carrying out the above plan of treatment, by exchanging his residence from London to Brighton, a gentleman who consulted me in the autumn of last year has succeeded in reducing the daily urinary flux from 90 ounces, with a specific gravity of 1015; to 60—70 ounces, with a specific gravity of 1015—16, whilst the excessive elimination of phosphoric acid is proportionately reduced. The improvement in his urinary symptoms only became definite since his removal to Brighton.

be warm, and the patient carefully guarded against cold, since in these cases a reduction of bodily temperature is always noted. When, in spite of the pursuance of these therapeutic and hygienic conditions, the diuresis and excretion of phosphoric acid continues, though the general condition of the patient may temporarily improve, there is reason to fear that phthisis will supervene, or that the disease may assume the features of saccharine diabetes.

APPENDIX

EFFECT OF BICARBONATE OF POTASH ON THE ACIDITY OF URINE

Thirty-two years ago Dr Bence Jones, in a paper read before the Royal Society,* showed conclusively, from a series of observations, that large doses of sesquicarbonate of ammonia not only did not diminish the acidity of the urine, but actually increased it; as he found that the day when most carbonate of ammonia was taken the acidity was higher than it had been any previous day, and that the acidity of the urine was still very high on the day following its discontinuance. Four years later a similar observation was made by Dr W. F. Beneke† with regard to the effect of bicarbonate of soda. And lastly, Professor Parkes,‡ in his work on the 'Urine,' published in 1860, instances a case of rheumatic fever in which the acidity of the urine on the day following the administration of bicarbonate of potash was considerably higher than on the day before it was taken.

It is strange that observations made by authorities so

* 'Philosophical Transactions,' 1850, part ii, p. 673.

† 'Archiv des Wissenschaftlichen Heilkunde,' 1854. 'Studien zur Urologie,' p. 444.

‡ 'Composition of the Urine in Health and Disease,' p. 297. Churchill, 1860.

eminent and trustworthy, tending to controvert the generally received opinion as to the action of these alkaline bicarbonates as antacids, and establishing the contrary proposition that they increase rather than diminish the acidity of urine, should have attracted so little the attention of writers on therapeutics or urinary pathology in this country or abroad.

As the question is of considerable importance with regard to treatment especially of those affections which are caused by the excessive formation of acid within the system, I have thought an account of some observations made by myself on the action of one of these carbonates—the bicarbonate of potash—would be of service, not merely in calling attention to an important therapeutic fact, but also in determining the circumstances that induce this apparently anomalous action, and in endeavouring to explain the paradox of these alkaline salts increasing instead of diminishing the acid reaction of the urine.

The first series of observations were made to test the effect of bicarbonate of potash on the reaction of the urine when taken before meals. The quantity of the salt taken was two drachms in the twenty-four hours—namely, one drachm at 12 p.m. (one hour before dinner), and one drachm at 8 p.m. (one hour before supper). The physiological conditions of food, rest and work were kept as equal as possible.

OBSERVATION 1.—Sept. 7th, 8th, 9th, 1876.

	Quantity. Cub. cent.	Acidity. Grm.	Uric acid. Grm.
Day before . .	. 1730	... 1·4	... 0·41
Day, with 2 drs. of bicarbonate	. 2080	... 0·78	... 0·66
Day after . .	. 1750	... 2·3	... 0·70

Observation 2.—Aug. 10th, 11th, 12th, 1877.

	Quantity. Cub. cent.	Acidity. Grm.	Uric acid. Grm.
Day before . . .	1442	2·5	1·05
Day, with 2 drs. of bicarbonato .	1720	1·2	0·75
Day after . . .	1230	3·9	1·7

Observation 3.—May 12th, 13th, 14th, 1878.

	Quantity. Cub. cent.	Acidity. Grm.	Uric acid. Grm.
Day before . . .	2050	1·9	1·05
Day, with 2 drs. of bicarbonate .	2190	1·2	1·6
Day after . . .	1650	2·4	1·3

In order to determine the effect of bicarbonate of potash on the hourly variations in the reaction of the urine, when taken before meals, two observations were made. In each instance, for the purpose of comparison, the variations of the acidity of the preceding day, when no bicarbonate was taken, are given.

Observation 1.

Day preceding experiment—Aug. 10th 1877.

	Quantity. Cub. cent.	Acidity. Grm.	Uric acid. Grm.
Water passed from 12 p.m. to 1 p.m.	58	0·9	·04
„ „ 1 p.m. to 2 p.m.	55	·08	·03
„ „ 2 p.m. to 3 p.m.	90	·08	·06
„ „ 3 p.m. to 4 p.m.	35	·07	·09
„ „ 4 p.m. to 5 p.m.	104	·17	·09
Total . .	342	0·39	0·31

Day of experiment—Aug. 11th, 1877.

	Quantity. Cub. cent.	Acidity. Grm.	Uric acid. Grm.
Water passed from 12 a.m. to 1 p.m.	72	Alkaline	·05
„ „ 1 p.m. to 2 p.m.	45	„	·04
„ „ 2 p.m. to 3 p.m.	40	·05	·08
„ „ 3 p.m. to 4 p.m.	70	·09	·08
„ „ 4 p.m. to 5 p.m.	90	·09	·07
Total . .	317	0·23	0·32

Observation 2.

Day preceding experiment—Nov. 6th, 1877.

	Quantity. Cub. cent.	Acidity. Grm.	Uric acid. Grm.
Water passed from 12 a.m. to 1 p.m.	34	·046	·04
„ „ 1 p.m. to 2 p.m.	43	·094	·06
„ „ 2 p.m. to 3 p.m.	41	·096	·03
„ „ 3 p.m. to 4 p.m.	50	·065	·04
„ „ 4 p.m. to 5 p.m.	60	·075	·03
Total . .	228	0·376	0·20

Day of experiment—Nov. 7th, 1877.

	Quantity. Cub. cent.	Acidity. Grm	Uric acid Grm.
Water passed from 12 p.m. to 1 p.m.	82	Alkaline	·07
„ „ 1 p.m. to 2 p.m.	60	„	·06
„ „ 2 p.m. to 3 p.m.	98	0·11	·04
„ „ 3 p.m. to 4 p.m.	150	0·13	·05
„ „ 4 p.m. to 5 p.m.	310	0·11	·07
Total . .	700	0·35	0·29

It will be gathered from these observations that though the acidity of the urine was depressed on the days the bicarbonate was taken, yet on the days following there was in each instance a considerable increase as

compared with the day preceding the experiment. Besides, the actual depression of the acidity on the days when the salt was taken is much less than might be expected, when we consider the neutralising effect such a quantity of an alkaline salt would have, and it is evident that a considerable quantity of free acid must have been passed into the urine after the immediate effect of the alkali had passed off, in order to have maintained this degree of acidity. How quickly the urine recovers its acidity is shown by the subsequent observations on the hourly variations of the reaction of the urine when the salt was taken before meals; the reaction in both instances never remaining alkaline more than two hours, whilst the acid passed in the remaining three hours amounts to little less than the acid excreted in the five hours on the day preceding the experiment. It will also be observed that the excretion of uric acid was increased on the days the bicarbonate of potash was taken.

A second series of observations were made to test the effect of bicarbonate of potash when taken after meals. The quantity of the salt taken was two drachms in twenty-four hours—viz. one drachm at 2 p.m. (one hour after dinner), and one drachm at 9 p.m. (one hour after supper). The physiological conditions of food, rest, and work were kept as equal as possible.

OBSERVATION 1.—Feb. 20th, 21st, 22nd, 1877.

	Quantity. Cub. cent.	Acidity. Grm.	Uric acid. Grm.
Day before . . .	1480	1·6	0·69
Day, with 2 drs. of bicarbonate .	1720	Neutral	0·76
Day after	2540	1·5	0·91

Observation 2.—May 2nd, 3rd, 4th, 1877.

	Quantity. Cub. cent.	Acidity. Grm.	Uric acid. Grm.
Day before . . .	2600	2·4	1·04
Day, with 2 drs. of bicarbonate .	1900	Neutral	0·95
Day after . . .	2300	1·3	1·15

Observation 3.—May 21st, 22nd, 23rd.

	Quantity. Cub. cent.	Acidity. Grm.	Uric acid. Grm.
Day before . . .	1290	1·3	1·7
Day, with 2 drs. of bicarbonate .	2600	Alkaline	2·1
Day after . . .	1480	1·7	1·8

The effect also of bicarbonate of potash on the hourly variation of the reaction of the urine was determined on two occasions; and for the purpose of comparison the variations of the acidity of the day preceding, when no bicarbonate was taken, are given.

Observation 1.

Day preceding experiment—Jan. 25th, 1878.

	Quantity. Cub. cent.	Acidity. Grm.	Uric acid. Grm.
Water passed from 1 p.m. to 2 p.m.	53	·06	0·12
„ „ 2 p.m. to 3 p.m.	55	·15	0·12
„ „ 3 p.m. to 4 p.m.	41	·11	0·11
„ „ 4 p.m. to 5 p.m.	60	·04	0·07
„ „ 5 p.m. to 6 p.m.	61	·02	0·12
Total . .	270	·38	0·54

Day of experiment—Jan. 26th, 1878.

	Quantity. Cub. cent.	Acidity. Grm.	Uric acid. Grm.
Water passed from 1 p.m. to 2 p.m.	47	·11	0·6
„ „ 2 p.m. to 3 p.m.	83	Neutral	0·6
„ „ 3 p.m. to 4 p.m.	103	Alkaline	0·7
„ „ 4 p.m. to 5 p.m.	105	„	0·3
„ „ 5 p.m. to 6 p.m.	110	„	0·7
Total . .	448	—	0·29

OBSERVATION 2.

Day preceding experiment—Feb. 20th, 1878.

	Quantity. Cub. cent.	Acidity. Grm.	Uric acid. Grm.
Water passed from 1 p.m. to 2 p.m.	55	·11	0·09
„ „ 2 p.m. to 3 p.m.	34	·02	0·04
„ „ 3 p.m. to 4 p.m.	94	Alkaline	0·10
„ „ 4 p.m. to 5 p.m.	50	·02	0·08
„ „ 5 p.m. to 6 p.m.	306	·08	0·06
Total . .	539	·23	0·37

Day of experiment—Feb. 21st, 1878.

	Quantity. Cub. cent.	Acidity. Grm.	Uric acid. Grm.
Water passed from 1 p.m. to 2 p.m.	15	·08	·04
„ „ 2 p.m. to 3 p.m.	92	Alkaline	·03
„ „ 3 p.m. to 4 p.m.	45	„	·09
„ „ 4 p.m. to 5 p.m.	65	„	·07
„ „ 5 p.m. to 6 p.m.	105	„	·06
Total . .	322	—	0·29

The effect, therefore, of bicarbonate of potash, taken after food, on the acidity of the urine, is different from that when it is administered before meals. For when taken on an empty stomach we have seen that the acidity on the day of administration was only slightly depressed, whilst on the day following the acidity was considerably higher than it was the day before the salt was taken. But when it was administered during the process of digestion the acidity of the urine entirely disappeared, being on two occasions neutral, and on one alkaline, whilst on the succeeding days there was no marked increased in the acidity of the urine as compared with that of the days preceding the experiment. And the same difference is observable in the hourly variations of

the urine, for when the bicarbonate was taken before meals the effects of the alkali passed off at the end of two hours, and the amount of acid passed in the succeeding three hours was nearly equal to what was passed on the day no medicine was taken; whilst when the salt was taken after meals the urine remained alkaline up to the end of four hours after the dose was taken, and no recovery of acidity was noticeable.

The result of these observations tends to establish the fact that the administration of an alkaline bicarbonate on an empty stomach increases the acidity of the system whilst its administration after a meal diminishes it.

The explanation as how it happens that these alkaline bicarbonates have such opposite effects will be found given at pages 55 and 56 of the text.

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